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# PULMONARY REST BY POSTURE[1]

PHILIP H. PIERSON AND R. R. NEWELL

The matter of pulmonary rest has long been our chief concern in the treatment of tuberculosis of the lungs. This has been accomplished by posture alone or with the aid of sandbags or other means of external compression, by slower and shallower respiration, by artificial pneumothorax, at times associated with open or closed pneumolysis, phrenic neurectomy or some form of thoracoplasty. The first thing generally to be considered is posture: Is there some position which may be assumed which will splint the lung and thereby give the diseased lung less work?

In 1916 and 1921, Webb, Forster and Houck (1) suggested that in their observations they had found that, if a patient lay upon the side of his diseased lung, in time it did less work than the lung which was uppermost. They recognized that at first (during the first hour so so) the diaphragm moved more on the down side, but they felt that after that time the action was reversed and it moved less on the down side. They also stressed the fact that when the mediastinum was flexible it dropped toward the down side, thus adding to the compression of that lung. And hence where there was diminished space, "decreased motion" and congestion, the tuberculosis had a better opportunity to heal.

Several factors determine upon which side a patient prefers to lie, namely, habit, the direction from which light comes, and so forth. Webb and his associates found that in a series of 529 healthy individuals the preference was as follows: 48 per cent preferred the right side; 23 per cent preferred the left side; 20 per cent slept on either side; 8 per cent preferred the back; and 1 per cent preferred the stomach.

## OUR OBSERVATIONS

After questioning a considerable number of patients with pulmonary tuberculosis, it was found that some had no preference as to position and that many preferred to lie upon the side of their good lung. It occurred to us that perhaps in these individuals this was demanded by nature and

[1] From the Departments of Medicine and Roentgenology, Stanford University Medical School, San Francisco, California.

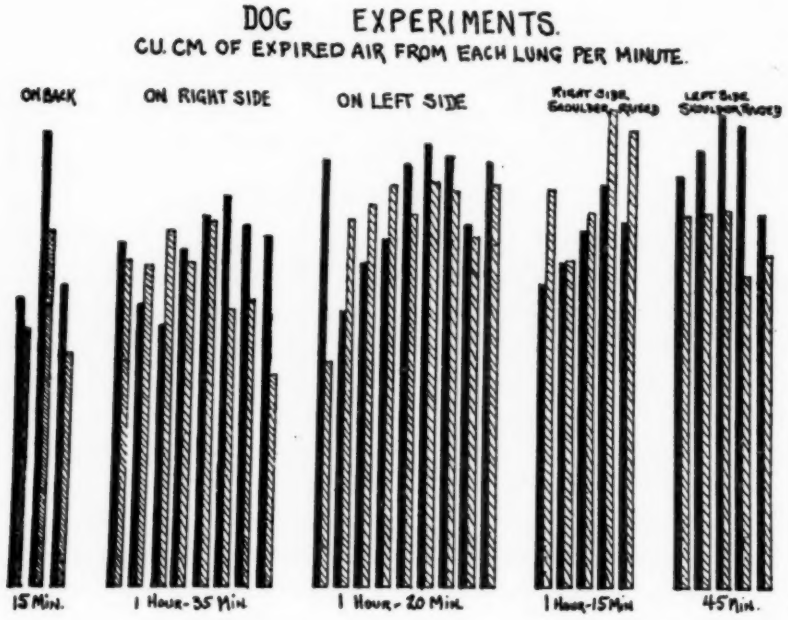


FIG. 1. Dog with cannula tied in each bronchus; air collected under water. The tidal air from the lung of the down side was greater than from the upper lung, especially when the shoulder was raised (simulating the position assumed by a patient reclining with head-rest elevated). The black columns show tidal volume from left lung, the hatched columns from right lung.

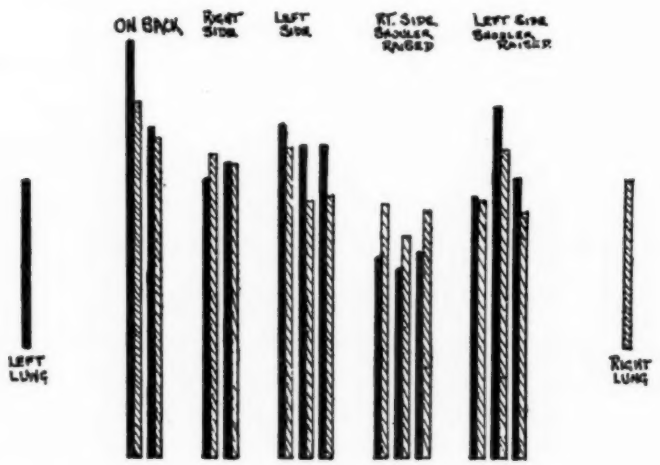


FIG. 2. Van Allen cannula used and air collected similarly. In each of the experiments the tidal air was greater in amount from the lung on the down side than from the upper lung.

that in that position there was a mechanism of splinting the uppermost lung. To determine what this was we made the following observations.

Three healthy medical students were studied by serial roentgenograms, each representing a double exposure,—one in normal inspiration and one in normal expiration, after varying lengths of postural rest on each side. It was found that there was (a) a fall of the mediastinum, (b) an elevation of the diaphragm on the down side, (c) increased pulmonary density on the down side commensurate with the compression due to (a) and (b), (d) a wider diaphragmatic excursion on the down side than on the up side, and (e) visible expansion of the ribs on only the up side. These conditions persisted as long as the experiments lasted.

This led to the question as to which was more important,—the increased diaphragmatic movement on the down side or the increased costal movement on the up side. Which lung was doing more work?

It might be well at this time to clarify certain terms, namely, work and rest. The lung, being largely a passive organ, really does very little work from the point of view of expending energy, but the term implies *motion*. The term *rest* may be defined as the absence of volumetric change.

The aforementioned question was first studied in dogs. In the first experiment a Van Allen cannula was used which collected the expired air from each lung separately (the dogs being under avertin anaesthesia). In the second experiment a glass cannula of good size was tied into the main bronchus of each lung and the lungs were so expanded that no pneumothorax persisted. We found more air expired from the lung on the down side, especially when the shoulders were elevated, simulating the position assumed by a patient with the head-rest of the bed raised.

This same problem was applied to two patients with complete thoracoplasties and one with a complete fibrothorax, knowing that their tidal air must all be limited to their one good lung. Roentgenograms, with superimposed shadows taken during inspiration and expiration, were checked by spirometric observations to be sure that our readings were being recorded for normal breathing, and also with Tissot measurements to observe the amount of air expired. It was found that when the good lung was down the mechanism of respiration was largely accomplished by the diaphragm, while if the collapsed lung was down breathing was accomplished by some action of the rib-cage with less motion of the diaphragm. As in normal individuals, the dome of the diaphragm occupied a position several centimetres more cephalad when on the down side than when on the up side. Our deduction from this was that the tidal air in the down

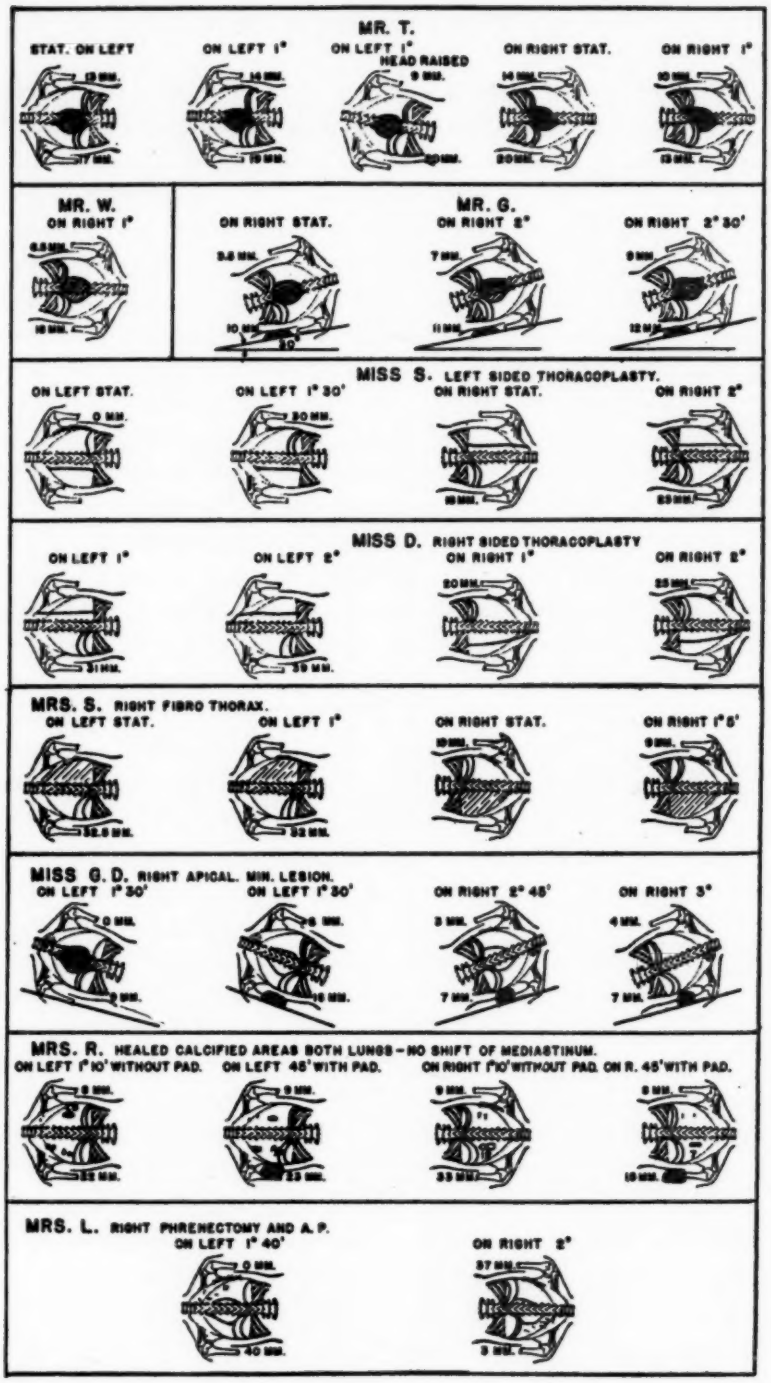
MR. T.
STAT. ON LEFT
ON LEFT 1°
ON LEFT 1° HEAD RAISED
ON RIGHT STAT.
ON RIGHT 1°
MR. W.
ON RIGHT 1°
MR. G.
ON RIGHT STAT.
ON RIGHT 2°
ON RIGHT 2° 30'
MISS S. LEFT SIDED THORACOPLASTY.
ON LEFT STAT.
ON LEFT 1° 30'
ON RIGHT STAT.
ON RIGHT 2°
MISS D. RIGHT SIDED THORACOPLASTY
ON LEFT 1°
ON LEFT 2°
ON RIGHT 1°
ON RIGHT 2°
MRS. S. RIGHT FIBRO THORAX.
ON LEFT STAT.
ON LEFT 1°
ON RIGHT STAT.
ON RIGHT 1° 5'
MISS G. D. RIGHT APICAL. MIN. LESION.
ON LEFT 1° 30'
ON LEFT 1° 30'
ON RIGHT 2° 45'
ON RIGHT 3°
MRS. R. HEALED CALCIFIED AREAS BOTH LUNGS – NO SHIFT OF MEDIASTINUM.
ON LEFT 1° 10' WITHOUT PAD.
ON LEFT 45' WITH PAD.
ON RIGHT 1° 10' WITHOUT PAD.
ON R. 45' WITH PAD.
MRS. L. RIGHT PHRENECTOMY AND A. P.
ON LEFT 1° 40'
ON RIGHT 2°

FIG. 3. Diagrammatic study of cases 1 to 9 showing motion of rib-cage, position and millimetres of motion of each leaf of the diaphragm after periods of rest. (The term 1° 30′ represents 1 hour and 30 minutes, 45′ represents 45 minutes, etc.)

lung, where the ribs were splinted, was almost completely moved by the increased motion of the diaphragm.

The question then arose as to how much of the down lung entered into this exchange of air: namely, was it the portion just above the diaphragm or was the action of this diaphragm transmitted to the cephalad portion as well? A patient was chosen who had had tuberculosis and in whom calcified areas were distributed in such a manner as to act as good markers of pulmonary movement. This study showed that the increased motion of the diaphragm on the down side was associated with wide movement of the calcification near the middle of the lung and quite definite movement as high as the clavicle. When the patient was turned, these same markers, now in the upper side, moved very little. This is in accord with the work of Macklin, *The Dynamic Bronchial Tree* (2), in which it was shown that the passive pulmonary structures followed the expansion and contraction of the thoracic walls and the diaphragm, and that this action, in a vertical plane, was evident at the hilum and even into the apex.

Still in search for the beneficial effect of resting the lung by posture, we took a patient with one side of the diaphragm paralyzed by a right phrenic neurectomy. She also had a selective collapse by pneumothorax of her right upper lobe. The mechanism of compensatory respiration was very striking. When lying on her good side, the diaphragmatic excursion was very great, carrying on most of the respiratory work. The upper, or diseased side, was only used to a slight degree and this was by a limited costal action. When she lay upon her operated side, the paralyzed diaphragm rose high (cephalad) into her right lung, was essentially immobile (3 mm. paradoxical motion), the rib-cage was splinted and in this case the down lung was rested more than in any of the other experiments. It would seem that this procedure, namely, with the patient lying on her diseased lung with the diaphragm paralyzed, does rest the down lung very nearly completely, whereas without the phrenic neurectomy the posture fails utterly.

Finally, we were interested in the length of time the above-described mechanisms persisted, that is, how long the diaphragm continued to show increased excursion on the down side. A patient at the San Francisco Hospital[2] was studied after lying upon one side for a period of two weeks. Even after this time it was seen that there was an increased excursion of the diaphragm on the down side as compared with its mate.

[2] City and County of San Francisco, Department of Public Health.

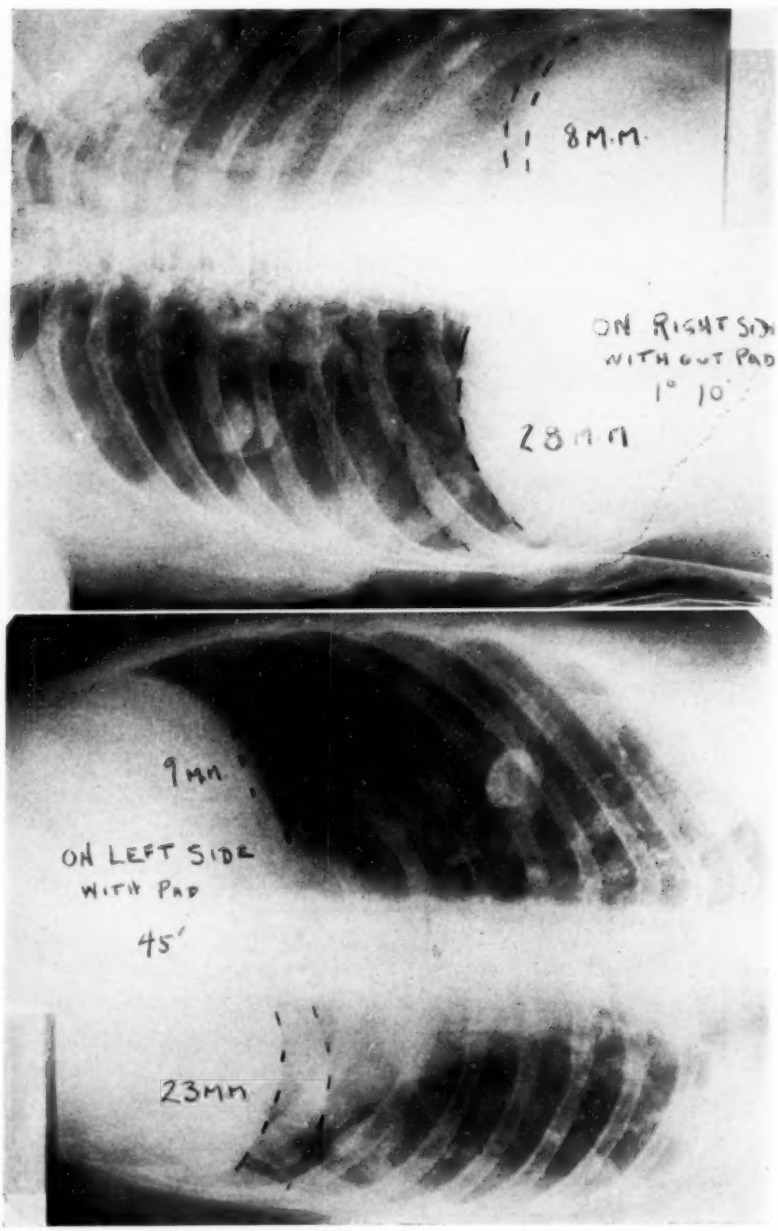


FIG. 4. Mrs. R.: Lying on right side. The right diaphragm when on the down side shows greater excursion than the left and this in turn is reflected into the lung by greater motion of the calcified marker in the midlung and blurring of the fibrous markings in the subclavicular region. When she lies on her left side, the markers (now in the upper lung) move very little, due to less motion of the right diaphragm.

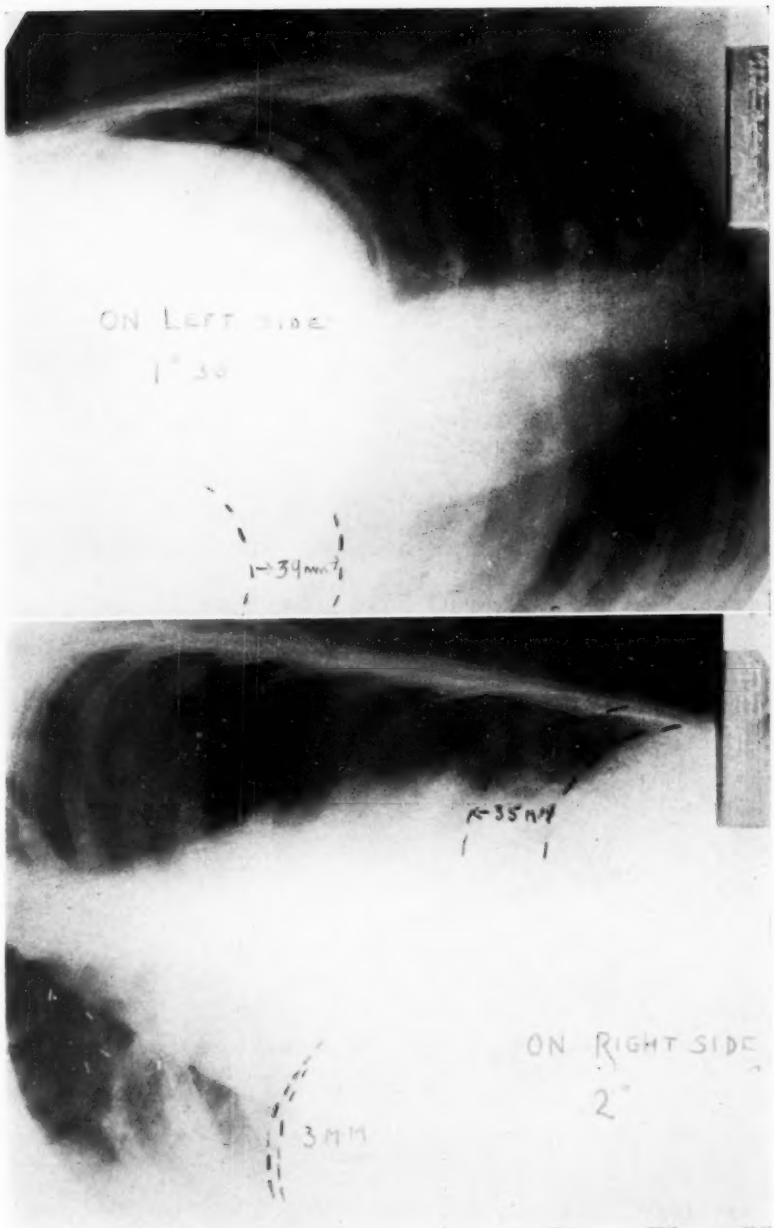


FIG. 5. Mrs. L.: Phrenic neurectomy and selective pneumothorax on right. When lying on her right side there was a marked cephalad position of the right leaf of her diaphragm, which was practically immobile (3 mm. of paradoxical motion) and no motion of the rib-cage on this side, due to pressure. This combination (phrenic neurectomy and lying on the diseased side) afforded the best of conservative means of resting one lung.

PHYSICAL EXPLANATION FOR THE ABOVE OBSERVATIONS

*1:* The mediastinum falls toward the down side according to its flexibility.

*2:* The (essentially hydrostatic) pressure of the abdominal viscera pushes the diaphragm cephalad on the down side, but exerts practically

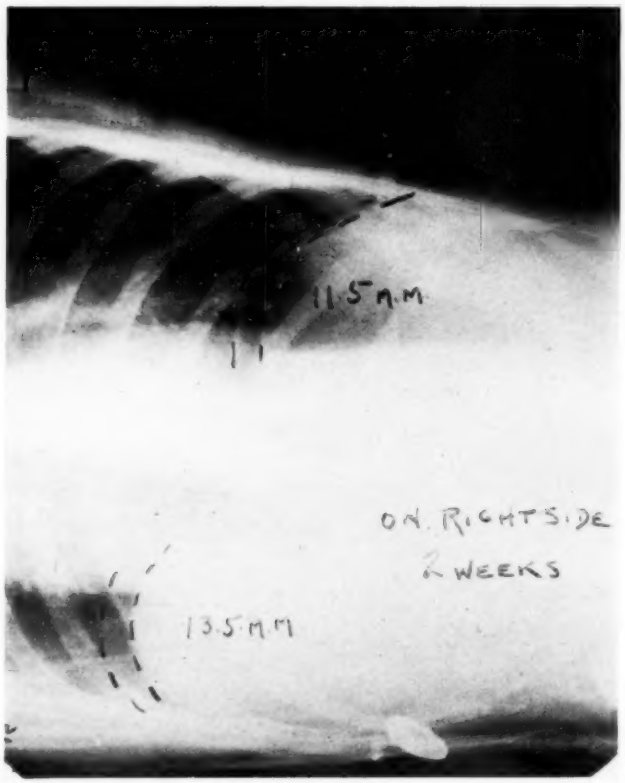


FIG. 6.: Mrs. S. F.: After lying on her right side for 2 weeks there was still more motion of the diaphragm on the down side.

no pressure cephalad on the up side (average 15 cm. water-pressure greater on the down side than on the up side).

*3:* The increased motion of the diaphragm on the down side is aided by the fact that a muscle under tension reacts more actively, inspiration being a thrust against the pressure of the abdominal contents. Quiet expiration is a passive motion. On the up side it is done by the elastic recoil of the lung which diminishes as the lung contracts. On the down

side it is done mostly by the subdiaphragmatic pressure of the abdominal contents, a force which continues practically undiminished no matter how far cephalad the diaphragm moves.

## CONCLUSIONS

1. As our chief aim in any treatment of tuberculosis is general as well as local rest, the patient should be allowed to recline in that position which affords the most rest to him. To say that if a patient lies upon one or the other side he automatically rests or splints the down lung is not borne out by these observations and the reverse seems to be the fact.

2. If rest of a lung is desired, it may be obtained by paralyzing the phrenic nerve and having the patient lie on that side.

3. The diaphragm moves more on the down side than on the up side and this relation persists as long as the lateral decubitus is maintained (two weeks in one patient).

4. If our experiments with dogs are sound, it is evident that there is not only more motion in the down lung but there is also more tidal air moved by that side.

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(1) Webb, G. B., Forster, A. M., and Houck, F. M.: Journ. Am. Med. Ass., 1916, lxvii, no. 20.

Webb, G. B., Forster, A. M., and Gilbert, G. B.: Ibid., 1921, no. 13.

(2) Macklin, C. C.: The dynamic bronchial tree, Amer. Rev. Tuberc., March, 1932, xxv, no. 3.

# THE INTERRELATIONSHIPS OF TUBERCULOSIS, SYPHILIS AND ANTISYPHILITIC TREATMENT[1, 2]

PAUL PADGET[3] AND JOSEPH EARLE MOORE

Interest in the interrelationships of diseases and their mutual interactions, one upon the other, has been reawakened in recent years by many clinical and experimental developments, the most dramatic of which is the effect of induced malaria upon syphilitic infection. It is apparently true that the association of two infections in the same individual may profoundly modify the usual course of one or both. The two most prevalent major infections of man are tuberculosis and syphilis. Their frequent coexistence raises important problems, particularly of prognosis and treatment, for physicians expert in both fields.

Most of the available discussion in the literature is limited to the association of pulmonary tuberculosis and syphilis, and centres around three questions: Whether either disease is more prevalent in patients infected with the other than in the population at large; whether the coexistence of the two alters the clinical course of either; and whether it is desirable to administer specific treatment to the syphilitic patient with tuberculosis, and, if so, in what form. Most studies, too, approach these questions from the point of view of the tuberculosis expert rather than from that of the syphilologist. It has seemed to us worth while, on the bases of a critical review of the literature and of a brief summary of our own experience, to indicate the differences in points of view of the sanatorium physician dealing with hospitalized patients, and of the syphilologist whose experience is with an ambulatory group; to reconcile these differences where possible; to review the hiatuses in our knowledge; and to suggest that the unsolved problems be approached by a coöperative effort of both fields of medicine.

[1] Presented before the Clinical Section at the thirty-first annual meeting of the National Tuberculosis Association, Saranac Lake, New York, June 24, 1935.

[2] From the Syphilis Division of the Medical Clinic, the Johns Hopkins Hospital, Baltimore, Maryland.

[3] Eli Lilly Research Fellow in Medicine.

## THE INCIDENCE OF COEXISTENCE OF SYPHILIS AND TUBERCULOSIS

The older literature, which is well summarized by Potter (1), contains many expressions of opinion. Most observers have agreed that syphilis and tuberculosis occur in the same patient more frequently than the individual incidence of the two diseases could explain, and have so postulated some inherent relationship in their biology.

Following the more universal application of the Wassermann reaction as a routine diagnostic measure, some investigators (2) (3) (4) (5) arrived at the same conclusion by comparing the frequency of syphilis in groups of tuberculosis patients with the estimated incidence of syphilis in the population at large. Others (6) (7), however, from the same approach, concluded that the reverse was true, that is, that syphilis was not more common among tuberculosis patients than in the general population. Such observations have no statistical value, because of the large errors

TABLE 1

*The incidence of syphilis observed at autopsy in tuberculous and nontuberculous individuals (after Landsberger)*

| 5,323 CASES | ACTIVE TUBERCULOSIS | FIBROID TUBERCULOSIS | ALL TUBERCULOSIS | NO TUBERCULOSIS |
|---|---|---|---|---|
| | 1,267 | 516 | 1,783 | 3,540 |
| Per cent with syphilis | 3.23 | 10.27 | 5.27 | 8.81 |

inherent in estimating the general incidence of syphilis and because of the small size, or the arbitrary selection, of the groups of tuberculosis patients considered.

Landsberger (8) examined the autopsy records of 5,323 patients. Table 1 shows the incidence of syphilis in patients with and those without tuberculosis. Of the patients who presented no evidence of tuberculosis, 8.81 per cent manifested anatomical lesions of syphilis, while such lesions were present in 5.27 per cent of those with tuberculosis. Only 3.23 per cent of the patients with active tuberculosis had syphilis, however, whereas 10.27 per cent of those with fibroid tuberculosis exhibited both diseases. In table 2 the same material is considered from the reverse standpoint of the incidence of tuberculosis in those with and those without syphilis. Twenty-three per cent of the patients with syphilis also had tuberculosis; in 10 per cent it was active and in 13 per cent it was fibroid in character. Thirty-four per cent of the nonsyphilitic patients

exhibited tuberculous lesions which were active in 25 per cent and fibroid in 9 per cent. From a complete analysis of this material, in which the age and sex of the patient and the type of syphilitic lesion presented were taken into consideration, Landsberger concluded that syphilis and tuberculosis do not coexist more frequently than their individual incidence might explain.

TABLE 2

*The incidence of tuberculosis observed at autopsy in patients with and without syphilis (after Landsberger)*

| TOTAL, 5,323 PATIENTS | ACTIVE TUBERCULOSIS | FIBROID TUBERCULOSIS | ALL TUBERCULOSIS |
|---|---|---|---|
| | *per cent* | *per cent* | *per cent* |
| With syphilis, 406 | 10.1 | 13.1 | 23.2 |
| Without syphilis, 4,917 | 24.9 | 9.5 | 34.4 |

TABLE 3

*The incidence of syphilis in tuberculous and nontuberculous individuals (after Greer)*

| RACE | NUMBER OF PATIENTS | | PER CENT WITH SYPHILIS | |
|---|---|---|---|---|
| | | | Tuberculous | Not tuberculous |
| White | Tuberculous | 630 | 9.7 | 5.8 |
| | Not tuberculous | 649 | | |
| Negro | Tuberculous | 160 | 39.3 | 21.0 |
| | Not tuberculous | 138 | | |
| Mexican | Tuberculous | 192 | 17.2 | 10.8 |
| | Not tuberculous | 175 | | |
| Total | Tuberculous | 982 | 15.8 | 8.9 |
| | Not tuberculous | 962 | | |

Greer's (9) material comprised 1,944 patients, who presented themselves to a tuberculosis clinic for diagnosis, and were carefully examined accordingly. Serological tests were done on all patients but the diagnosis of syphilis was not otherwise considered. Half of the patients had clinically demonstrable tuberculous lesions; the remainder were adjudged nontuberculous. Table 3 presents the observed incidence of positive serological tests for syphilis in the tuberculous and nontuberculous groups. For each race, and so for the group as a whole, the incidence of syphilis

was conspicuously higher in those with tuberculosis (15.8 per cent) than in those without it (8.9 per cent). Since the groups were made up of individuals of comparable age, race and social status, Greer arrived at conclusions opposite from those of Landsberger.

In his study of the diagnoses of ten thousand patients admitted to the Syphilis Clinic of the Johns Hopkins Hospital, Turner (10) found that only 1.6 per cent of the negroes with syphilis also had pulmonary tuberculosis, whereas, he states, its incidence among the negroes of Baltimore, of whom the clinic patients are typical, was 2.61 per cent during a typical year of that period.

Table 4 presents a comparison of the incidence of syphilis and tuberculosis in 6,000 consecutive admissions to the Medical Wards of the Johns Hopkins Hospital. There were 1,171 patients (19.51 per cent) discharged with a diagnosis of syphilis, but in many of these the disease was

TABLE 4

*The incidence of syphilis, tuberculosis, and the coëxistence of the two diseases in 6,000 consecutive admissions to the Medical Service of the Johns Hopkins Hospital*

| | TOTAL | WITH SYPHILIS | WITH TUBERCULOSIS | EXPECTED INCIDENCE OF COEXISTENCE | OBSERVED INCIDENCE OF COEXISTENCE |
|---|---|---|---|---|---|
| Number of patients | 6000 | 1171 | 356 | 70— | 51 |
| Per cent | 100 | 19.51 | 5.93 | 1.16 | 0.85 |

latent, and the diagnosis rested solely upon the routine discovery of a positive blood-Wassermann reaction. Tuberculosis was diagnosed in 356 (5.93 per cent) of this same group; but in every instance upon the basis of definite clinical manifestations. Fifty-one of these patients (0.85 per cent) had both syphilis and tuberculosis, whereas, in the normal operation of the laws of chance, it would have been expected that 1.16 per cent would have manifested both diseases.

From the foregoing, one is tempted to conclude that syphilis and tuberculosis affect the same patient less frequently than would be expected on the basis of the general incidence of the two diseases, but, actually, critical examination reveals that none of these studies, including our own, can supply an accurate estimate of the presence or absence of a correlation in the occurrence of the two. Conclusions drawn from the study of autopsy material suffer from the fact that, whereas even minimal tuberculosis is relatively easy to detect at the section, syphilis manifests itself

in ways usually recognizable anatomically only late in the course of the disease, and then often only to the experienced eye.

Clinically the converse is true. Neglecting the refinements in history-taking and examination practised by the expert, the diagnosis of syphilis is still to be made with a high degree of accuracy (about 90 per cent) by routine serological tests alone, while the clinical diagnosis of pulmonary tuberculosis is reached only in the presence of outspoken activity or extensive fibroid changes, and even X-ray diagnosis is far from infallible. In the relative ease or difficulty of clinical or necropsy recognition of these two infections lies the difficulty in any attempt at statistical correlation of their incidence.

Before such correlation be considered valid, it is necessary that the following conditions of observation be satisfied:

*1:* The study should be based upon a large series of individuals, including the three groups of those clinically well, patients ill with pulmonary tuberculosis, and patients known definitely to have syphilis.
*2:* The incidence of syphilis should not be based upon routine serological tests alone, but should be determined by the evaluation of careful history, complete physical examination, and the appropriate serological tests by one well-schooled in clinical syphilology, and a careful classification of the types of the disease should be drawn.
*3:* The incidence of tuberculosis should be as carefully determined by one expert in this field, and every effort made to classify not only the stage of activity in those clinically ill, but also the presence and extent of a primary focus of infection, as judged by quantitative tuberculin reactions, stereoscopic chest rentgenograms, and clinical observation over a long period of time.
*4:* With these desiderata satisfied for a large group of patients, correlations should be attempted only with regard for the age, race, and sex of the patient groups, and with reference to the type, duration, and severity of the tuberculous and syphilitic infections.

## THE INFLUENCE OF TUBERCULOSIS ON THE COURSE OF SYPHILITIC INFECTION AND OF SYPHILIS ON THE COURSE OF TUBERCULOUS INFECTION

Attempts to evaluate the interaction of these two diseases in human beings are doomed to failure, by the very nature of the case. There are numerous clinical impressions, for instance, Schlesinger (7) (11) (12), Orszagh (5), and others, to the effect that active tuberculosis seems to modify in a favorable direction the course of syphilitic infection, and,

conversely, Giese and McGovern (13), Gallant (14), and Habliston and MacLane (15), that untreated syphilis affects unfavorably the course of tuberculosis. The latter assumption is better supported by the observed facts, and certainly better documented, than the former.

In effect, the data upon which most observers draw conclusions are based, not on the mutual interaction of tuberculosis and syphilis, but of tuberculosis and syphilis plus antisyphilitic treatment, a point first clearly stated by Sergent (16). There is no specific treatment for tuberculosis except rest; and "cure" is accomplished, as Petersen and Hecht (17) point out, by the process of walling off the tuberculous lesion. For syphilis, on the other hand, there are powerful specific remedies, all of them poisons, which bring about cure, if at all, by the complete eradication of foci of organisms and of syphilitic inflammatory tissue and its replacement by scarring, rather than by the walling-off process. There are few if any syphilitic patients who escape some drug therapy, and the effect of this on coexisting tuberculosis is likely to be as important as, or even more so, than the effect of the syphilitic infection.

One turns, therefore, to animal experimentation, in which the factor of treatment may be eliminated, for accurate information as to the effect which one of these infections has on the course of the other. Ohnawa (18) states, in a brief report in which protocols are not included, that rabbits previously infected with tuberculosis have a general increase in resistance to syphilis, and that the testicular tuberculosis in syphilitic rabbits progresses more rapidly than in controls.[4] This unsatisfactory report, and the as yet unpublished studies of Aronson, are the only experimental approaches to the problem with which we are familiar. The value of such a study as applied to man is dubious, however, because of the dissimilarity of both infections in man and experimental animals, and the relatively short life, and therefore short observation period, of the latter.

Even though the factor of antisyphilitic treatment modifies the picture in man, much is still to be learned by further studies similar to, but more extensive than, those already initiated by several observers, from the tuberculosis standpoint, but unfortunately by none from the point of

[4] One would expect this to be true from the work of Sabin, Cunningham, Morgan, and their collaborators. These investigators found that, while tuberculosis causes an increase of the phagocytic cells in the tissues, it depresses their physiological activities. Syphilis, while causing a similar increase in the same cells, increases their activity. On this basis, the coexistence of the two infections might provide an excessive number of cells capable of intracellular infection with, but not the destruction of the tubercle bacillus, and hence a spread of the tuberculous infection.

view of syphilis, namely, a comparison of the clinical course and ultimate outcome of either infection in patients with and without the other, taking into consideration the collateral factors outlined in the preceding section, and, in addition, the all important factor of antisyphilitic treatment.

### THE EFFECTS OF ANTISYPHILITIC TREATMENT ON THE COURSE OF TUBERCULOUS INFECTION

The divergent opinions of the pre-arsphenamine era as to the possible effect of mercury on the course of tuberculosis are now of academic interest only, since this drug has almost disappeared from syphilotherapy.

As for the iodides, a few workers, most recently Schlesinger (11), believe them to be beneficial rather than harmful; and Schlesinger goes so far as to advise daily intravenous injections of 10 gm. of sodium iodide as the ideal treatment of syphilis in a patient ill with pulmonary tuberculosis. Most observers, however, avoid the use of iodides, basing their fear on the old and well-known clinical observation that the administration of iodine to a tuberculous patient may cause the appearance of tubercle bacilli in sputum previously bacilli-free; on the classical experiments of Jobling and Petersen (22) on the effect of iodides on the ferment-antiferment balance of the blood; and upon the observations of Butler (23) that the administration of iodine or iodides to tuberculous guinea pigs caused them to die more quickly from tuberculosis than similarly infected controls.

With the introduction of arsphenamine, Ehrlich (19) stated, "Tuberculosis, when it has not progressed too far, offers no contraindication [to arsphenamine]; not only is there good effect upon the syphilis, but nonspecific improvement is also obtained." Herxheimer and Altmann (20) (21) substantiated Ehrlich's view; but it remained for Potter (1) to point out that, "The more active the tuberculosis, the smaller should be the initial dose [of an arsphenamine]; the slower its increase, the less frequent the interval, and the greater care and watchfulness required."

The nonspecific effect of the arsphenamines on tuberculous lesions is best shown in visible skin lesions of certain types. According to Stokes (24),

> In tuberculids the action [of the arsphenamines] is fairly constant and improvement takes place at a uniform rate, suggesting the action of treatment in syphilis, though somewhat slower. In tuberculous processes in the glands, throat, and skin, in the order named, there is less assurance of good effect.

In [tuberculous] multiple arthritis, periostitis, and osteitis, the effect is secured occasionally but not frequently. In uveitis the results secured depend on the age of the process. . . . The healing of tuberculids and erythema induratum is accomplished in from six to eight weeks and in more than 50 per cent is apparently permanent. . . . Sarcoids may require treatment for two or three courses. . . . Flare-ups or therapeutic shocks in tuberculous processes and uveitis occur.

Similar experiences have been reported by Herxheimer and Altmann (20) (21).

It is distinctly more difficult and perhaps impossible to measure so accurately the effect of the arsphenamines on tuberculous lesions in the lung. However, in more recent years, a number of reports have appeared

TABLE 5

*The outcome of the tuberculosis in 501 patients with both syphilis and tuberculosis in reference to antisyphilitic treatment (after Habliston and McLane)*

| TYPE OF SYPHILIS | TREATMENT FOR SYPHILIS | TUBERCULOSIS UNIMPROVED | UNIMPROVED OR DEAD |
|---|---|---|---|
| | | *per cent* | *per cent* |
| No syphilis: 3,962 patients | — | 25 | 75 |
| Latent: 231 patients | No | 20 | 80 |
| | Yes | 25 | 75 |
| Active: 270 patients | No* | 27 | 76 |
| | Yes | 39 | 61 |

* The figures given for this column in the original report are: Improved, 27.4 per cent; unimproved, 18.8 per cent; and died, 57.5 per cent, a total of 103.7.

concerning the effects of antisyphilitic treatment upon the course of events in patients with both syphilis and pulmonary tuberculosis.

Habliston and McLane (15) observed the course of events in 4,621 patients with tuberculosis, 659 of whom also had syphilis. Table 5 compares the end results of 501 of the patients with both infections with the outcome of those with tuberculosis alone, and demonstrates the different results obtained in those treated for syphilis, and those allowed to go without antisyphilitic therapy.

Twenty-five per cent of those with tuberculosis alone were improved, while during the period of observation 75 per cent were unimproved or dead. Two hundred and thirty-one patients were classed by them as "latent syphilis;" of those who received no antisyphilitic treatment, 20 per cent were improved and 80 per cent were unimproved or dead. Of

those who received treatment for syphilis in addition to the usual sanatorium care for tuberculosis, 25 per cent were improved and 75 per cent were unimproved or dead. There was thus no appreciable difference in the outcome of the tuberculosis in these three groups.

However, 270 patients were classified as "active syphilis" (type of activity and stage of syphilitic disease not stated). Of those who received no antisyphilitic treatment, 27 per cent[5] were improved and 76 per cent[5] were unimproved or dead; while of the group who were given antisyphilitic treatment 39 per cent were improved and 61 per cent were unimproved or dead. Thus, in their experience, the outlook for patients with tuberculosis and syphilis could be improved by the administration of

TABLE 6

*The outcome of tuberculosis in patients with both syphilis and tuberculosis in reference to antisyphilitic treatment*

| AUTHOR | TREATMENT FOR SYPHILIS | NUMBER OF PATIENTS | TRUBECULOSIS IMPROVED | DIED OR TUBERCULOSIS UNIMPROVED |
|---|---|---|---|---|
| | | | *per cent* | *per cent* |
| Giese & McGovern | No | 43 | 49 | 51 |
| | Yes | 54 | 63 | 37 |
| Gallant | No | 230 | 21 | 79 |
| | Yes | 116 | 51 | 49 |
| Sullivan | No | 66 | 11 | 89 |
| | Yes | 50 | 20 | 80 |
| Total | No | 339 | 22 | 78 |
| | Yes | 220 | 47 | 53 |

antisyphilitic treatment; slightly or negligibly so in those with latent syphilis, but more definitely so if the syphilitic process were active.

Similar reports have been presented by Giese and McGovern (13), Gallant (14), and Sullivan (25), whose results are summarized in table 6. In so far as such reports are comparable, the results are the same, and those who received antisyphilitic treatment did better, as judged by the manifestation of tuberculous activity, than those who did not. Consolidating these series, there were 339 patients with both syphilis and tuberculosis who received only the usual treatment for tuberculosis, and

[5] The figures given in the original report for this group were: Improved, 27.4 per cent; unimproved, 18.8 per cent; and died, 57.5 per cent—making a total of 103.7 per cent.

220 who, in addition, received some antisyphilitic therapy. Twenty-two per cent of the former were improved, and 78 per cent were unimproved or dead; while 47 per cent of the latter were improved, and only 53 per cent were unimproved or dead.

Gallant (14) went further, and, by classifying the tuberculous lesions which his patients manifested, demonstrated that antisyphilitic therapy is beneficial, no matter what the type of coexisting tuberculous lesion, provided the patient be not virtually moribund, but that the benefit is particularly striking if the tuberculosis be class B or less in activity.

None of these four reports, valuable as they may be from the standpoint of tuberculosis, provide essential information as to the syphilitic infection. No clear distinction is drawn between early or late syphilis, or the various types of the latter, and no information is provided as to the subsequent course of syphilis.

Throughout these reports, and in many others which are similar but less definitive, antisyphilitic treatment has been given according to the suggestions for caution made by Potter (1), and short courses of small doses of an arsenical have been alternated with interim heavy metal or with rest-periods. A usual scheme has been 6 doses of 0.3 gm. neoarsphenamine at weekly intervals alternating with a course of mercury by inunction and followed by a rest-period before resumption of arsenical therapy.

Such mild treatment, while of benefit to the allergic inflammatory lesions of patients with late syphilis, cannot be considered even palliative for certain forms of neurosyphilis, for example, and, according to present standards (26), it is totally inadequate for the "cure" of early syphilis, and in many instances for the prevention of infectious relapse.

## COMMENTS ON CURRENT TREATMENT METHODS OF THE COMBINED INFECTIONS

Current practice in the therapy of tuberculosis and syphilis complicating each other follows fairly closely the ideas of Schlesinger (12), who considers the question under four headings. The following four paragraphs are as nearly as possible in Schlesinger's words:

*1: Late syphilis, nonprogressive clinically, complicated by recent pulmonary tuberculosis:* The tuberculous process takes precedence; antisyphilitic treatment should be delayed until the tuberculous lesion has been stationary for several months, and then should be limited to the use of heavy metals, avoid-

ing the arsphenamines and the iodides. The tuberculosis may be treated in any manner desired, as in a nonsyphilitic patient.

*2: Untreated late syphilis with old fibroid pulmonary tuberculosis:* Activation of fibroid lesions by syphilis (or by its treatment) is less to be feared than with the exudative type. Arsphenamine may be used in addition to the heavy metals, but in small doses only. The risk of fever therapy (malaria) is unjustifiable except in paresis, or in other types of neurosyphilis, unless the tuberculous lesion is old, small, and well fibrosed.

*3: Old stationary pulmonary tuberculosis with early syphilis:* If the pulmonary lesion is fibroid, arsphenamine may be given without hesitation. If cavities are present, small doses only should be used at the start, increasing only if no progression of the lung lesion occurs. Schlesinger says: "*A number of experienced lung specialists, such as Schröder, Nicol, Harms, Treupel, and Schmidt, have observed the dissemination of tuberculosis, or haemoptysis after arsphenamine* [no references provided]. *I have several times seen rapid progress of pulmonary tuberculosis after salvarsan. Not only recent, but also older exudative processes are particularly endangered by salvarsan.*"

*4: Early syphilis with recent tuberculosis:* This is by far the most unfavorable combination of all. Although there are urgent reasons for the immediate treatment of syphilis, drug therapy must usually be limited to the heavy metals, for the reasons given in italics in the paragraph above. "Severe forms" (Schlesinger) of early syphilis, especially malignant syphilis, demand the use of arsphenamine even in usual doses; but in patients with "moderate skin eruptions" and in poor general physical condition, it is wise to wait for improvement in and convalescence from the tuberculosis before beginning antisyphilitic treatment.

Generally speaking, these instructions take the position that, to the patient, tuberculosis is more important and more dangerous than syphilis; and recognize the fact that, while none of the therapeutic measures currently used for tuberculosis will adversely affect syphilis, some of those used for syphilis may seriously modify the course of tuberculosis. While the latter point is true, the former is not necessarily so, and, with either disease, it does not suffice for the physician to consider the individual patient to the exclusion of the public health. Both syphilis and tuberculosis are communicable diseases; in both, contacts must be examined; in both, the spread of infection must be prevented if possible. With open tuberculosis this latter is gradually accomplished by the same method which provides individual treatment for the patient, that is, to place him at rest in bed in a sanatorium. In recent syphilis, with infectious lesions actually or potentially present, noninfectiousness must be

promptly achieved, even at some risk to the individual patient, by the administration of an arsphenamine. This is particularly true since, in actual practice, the tuberculosis sanatoria, especially those for negroes (in whom syphilis is widespread), are so crowded that a delay of weeks or even months after the diagnosis of tuberculosis may ensue before hospitalization and isolation can be accomplished. Under these circumstances, it is imperative that early syphilis be rendered noninfectious as promptly as possible.

From the standpoint of the individual patient, tuberculosis is not always a more serious disease than syphilis. There are types of late syphilis more surely fatal if untreated than even exudative tuberculosis (for instance, aortic regurgitation, aneurysm, paresis); and other types more productive of chronic invalidism than tuberculosis (for instance, tabes dorsalis and other forms of neurosyphilis). Even in a symptomless patient apparently clinically well, the expert syphilologist can often predict with confidence that grave forms of cardiovascular or neurosyphilis will develop in the future if treatment is withheld, and can guard against these developments with appropriate therapeutic methods.

While such general rules as Schlesinger lays down may be therefore applicable to the average patient, they are far from universally so. The solution of the problem of treatment of the combined infections should, in our opinion, be on an individual, rather than on a general basis. It should depend on an exact evaluation of the type and extent of anatomical and physiological damage done by each infection, utilizing all available diagnostic laboratory aids; on an expert estimate of the probable immediate and remote prognosis of each infection; and on cautious trial of the patient's tolerance for antisyphilitic drugs. To answer the questions: Which infection endangers the patient's life or health immediately? Which 20 years hence? What can he tolerate as to chemotherapy for syphilis?—demands the coöperative services of experts in both fields.

### THE EXACERBATION OF LATENT TUBERCULOSIS AS A RESULT OF ANTISYPHILITIC TREATMENT

Our own experience with tuberculosis combined with syphilis is gathered not under sanatorium conditions, but in a large ambulatory clinic, which deals with all manifestations of syphilis from the chancre to paresis. In each patient a general medical history is followed by a complete physical examination carried out before treatment. In the majority of patients with late syphilis (that is, of more than four years' duration),

| CASE NUMBER | HISTORY NUMBER | AGE | SEX | RACE | TYPE OF SYPHILIS | HISTORY SUGGESTING TUBERCULOSIS | P. E. OTHER THAN SYPHILIS | X-RAY OF CHEST |
|---|---|---|---|---|---|---|---|---|
| 1 | U14839 | 21 | F | C | Tertiary bone, periostitis | Yes | 0 | Enlarged root shows |
| 2 | U40001 | 27 | F | C | Latent | Yes | 0 | N.D.* |
| 3 | U44184 | 49 | F | C | Asymptomatic neurosyphilis | No | 0 | Lungs clear |
| 4 | U45124 | 32 | F | C | Latent | Yes | 0 | Lungs clear |
| 5 | U46323 | 19 | F | C | Latent | Yes | 0 | Lungs clear |
| 6 | U47556 | 26 | M | C | Latent | Yes | 0 | N.D. |
| 7 | U48057 | 40 | M | C | Latent | Yes | 0 | Lungs clear |
| 8 | U50443 | 17 | F | C | Secondary | Yes | 0 | N.D. |
| 9 | G44070 | 17 | F | C | Secondary | Yes | Bilateral cervical adenitis; otherwise 0 | Lungs clear |
| 10 | G62455 | 43 | M | C | Tabes dorsalis | No | 0 | Lungs clear |
| 11 | G63276 | 72 | M | C | Tertiary skin and bone; gumma of sternum | Yes | 0 | Lungs clear |
| 12 | H1702 | 17 | F | C | Secondary | Yes | Fibroid tbc., left apex | Fibroid tbc., apex |
| 13 | H4969 | 47 | F | C | Neurosyphilis | Yes | 0 | Lungs clear |
| 14 | H5208 | 19 | F | C | Latent | Yes | 0 | Lungs clear |
| 15 | K49965 | 16 | F | C | Secondary | Yes | 0 | Lungs clear |

* N.D. = No data.
c. = Courses.
** Total dosage in grams. Figures in parentheses refer to number of injections.
As = Arsphenamine (606).
Neo = Neoarsphenamine.
T = Tryparsamide.
Hg = Mercury.
Bi = Bismuth.

TABLE 7

| RAY OF CHEST | ANTISYPHILITIC TREATMENT** | INTERVAL FROM BEGINNING TREATMENT TO DEVELOPING SYMPTOMS OF TUBERCULOSIS | TYPE OF TUBERCULOSIS | OUTCOME |
|---|---|---|---|---|
| rged root shadows | As. 2.0 (8)<br>Bi 0.6 (3) | 3 months | Exudative pul. tbc., right apex | Died, pul. tbc. |
| * | Neo 1.8 (3)<br>Bi 0.2 (1) | 2 months | Tuberculous polyserositis | Died—autopsy |
| s clear | As 2.4 (8)<br>Bi 0.6 (3) | 2 months | Exudative pul. tbc., bilateral | Died, pul. tbc. |
| s clear | As 3.6 (12)<br>Bi 2.0 (10) | 6 months | Exudative pul. tbc.; tuberculous meningitis | Died—autopsy |
| s clear | As 0.3 (1) | 1 week | Miliary tbc.; tuberculous meningitis | Died—autopsy |
| | As 2.4 (8)<br>Bi 1.0 (5) | 4 months | Exudative pul. tbc., left upper | Died—autopsy |
| s clear | As 0.6 (2) | 2 weeks | Exudative pul. tbc., right apex | Tbc. arrested; syphilis arrested; working |
| | As 2.0 (7) | 2 months | Exudative pul. tbc., bilateral | Died, pul. tbc. |
| s clear | As 2.0 (8) | 6 weeks | Exudative pul. tbc., bilateral | Died, pul. tbc. |
| s clear | Neo 9.8 (20)<br>Hg rubs 2 c.*<br>T 10.0 (10) | 1 year | Miliary tbc. | Died—autopsy |
| s clear | As 1.2 (6) | 2 months | Miliary tbc. | Died |
| oid tbc., left ex | As 0.9 (3) | 6 weeks | Exudative pul. tbc., left upper | Died—autopsy |
| s clear | As 1.3 (6) | 6 weeks | Exudative pul. tbc., bilateral | Died at home |
| s clear | As 0.9 (3)<br>Neo 10.3 (16)<br>Hg rubs 1 c. | 3 months | Exudative pul. tbc., bilateral | Died |
| s clear | As 1.5 (5)<br>Neo 1.8 (3)<br>Bi 1.0 (5) | 1 month | Exudative pul. tbc., bilateral | Under observation |

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this is supplemented by a teleroentgenogram, performed because of our interest in the early diagnosis of uncomplicated syphilitic aortitis, but also offering, of course, an opportunity for the X-ray diagnosis of pulmonary tuberculosis, clinically unrecognized. Patients with obvious tuberculosis of the exudative type are transferred to sanatorium care as promptly as possible, so that their subsequent antisyphilitic treatment is almost entirely out of our hands. Those with recognizable closed fibroid tuberculosis are managed in accordance with the principles of the preceding section.

Our particular interest has been aroused, however, by a number of patients in whom tuberculosis, presumably present on admission, though latent, quiescent, and unrecognizable clinically or by X-ray, has flared into activity after the initiation of antisyphilitic treatment. In these patients the course of events was similar to that briefly mentioned by Schlesinger (*vide supra*) and the observers quoted by him.[6]

Included in our files are 242 patients with syphilis who had pulmonary tuberculosis on admission, or who developed tuberculosis under observation. Of these, there are 15 individuals in whom the sequence of events was such as strongly to suggest that the administration of an arsphenamine had provoked the flare-up and rapid dissemination of a previously quiescent and, we believe, clinically unrecognizable pulmonary tuberculosis. There were other instances in which the same seemed to be true, but which are not included here because of lack of definitive information.

Table 7 summarizes the salient features of this group. Most of the patients were young, three fifths of them were under thirty, and the majority of them were women. All were negroes. Two-thirds of the group had either early or latent syphilis; the others manifested a variety of late lesions. The admission physical examination revealed abnormalities other than the lesions of syphilis in only two: case 9 had bilateral cervical adenitis which was suspected of being tuberculous, and case 12 had definite fibrosis at the apex of the left lung. Twelve patients had roentgenograms of the chest done upon admission; in eleven no abnormalities were detected. In case 12 the clinical diagnosis of apical fibrosis was confirmed.

A noteworthy feature is that, in reviewing the recorded histories of these patients, taken in every instance weeks or months before a diagnosis

[6] Similar cases have been reported by Levi-Valensi, A.: *Bull. & Mém. Soc. Méd. Hôp. Paris*, 1934, I, 1466; by Laederich, L., & Weil-Spire, R.: *Ibid.*, 1926, I, 949; and by Mauradin, Ann. d. Mal. Vén., 1924, vi, 19.

of pulmonary tuberculosis was made, all but two were found to have given a history which might have suggested the possibility of pulmonary tuberculosis, such as rapid weight-loss, general constitutional symptoms of fatigability, malaise, or a sensation of fever, bouts of chest pain, cough, or night-sweats. Such symptoms, especially when vague, may be caused by any constitutional disease, including syphilis, but it is our impression that their uniform occurrence in this group of patients is of significance.

All patients received an arsphenamine, usually old arsphenamine, in weekly doses of 0.3 or 0.4 gm.; and in the majority the course of events was monotonously the same. At a variable interval, usually about the end of the first course of arsphenamine, and within three months of the beginning of treatment in all but two instances, the patient complained of classical symptoms of pulmonary tuberculosis. Examination revealed extensive pulmonary changes which were confirmed by roentgenogram, and after a rapidly downward course, death ensued from tuberculosis.

In case 3, examination done upon admission and again eighteen months later, after a lapse without treatment, revealed no signs of tuberculosis, yet death occurred from pulmonary tuberculosis four months after beginning intensive antisyphilitic treatment. The rapid development of fatal miliary tuberculosis with tuberculous meningitis in case 5, suggests that dissemination had begun before the one dose of arsphenamine was given, but acute symptoms developed only after the treatment.

Case 7 represents the only instance in this group of arrest of the tuberculous process once symptoms were apparent. Following the second injection of arsphenamine, the patient complained of distressing symptoms. Reëxamination revealed a rapidly developing pulmonary tuberculosis; the patient was hospitalized; the antisyphilitic therapy was continued in a greatly modified fashion; and for almost three years neither process has advanced.

Case 10 falls into a special category. His course was uneventful until the development of thrombocytopoenia after an injection of neoarsphenamine; following this, perhaps as a result of lowered defense mechanisms, he developed miliary tuberculosis, with the usual fatal result.

Cases 4 and 15 are here reported in more detail, as being typical of the group.

*Case 4:* A. W. Unit 45,124. This colored woman of 32 was admitted to the Johns Hopkins Hospital on August 31, 1932, complaining of tightness in the

chest. Her past health had been good. Her illness had begun seven months before with a "cold on the chest" and cough, and, although the cough had abated, a feeling of tightness in the chest had remained, and she had felt ill. There had been, over this period, a loss of about 70 lbs. in weight. Upon ex-

FIG. 1

FIG. 2

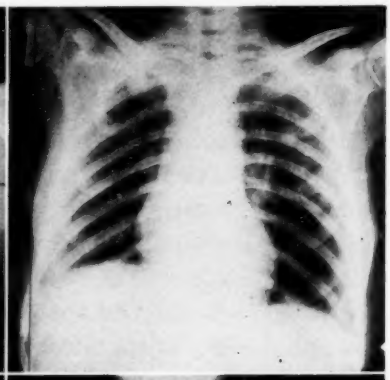

FIG. 3

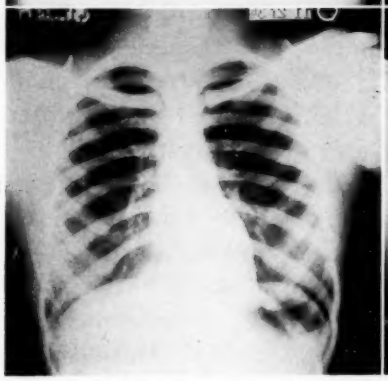

FIG. 4

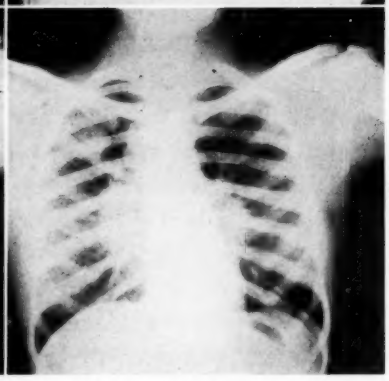

FIG. 1. A. W. Roentgenogram of chest September 1, 1932. Lungs clear except for moderate fibrosis at right hilum.

FIG. 2. A. W. Roentgenogram of chest May 1, 1933. Note extensive seeding infiltration in upper halves of both lungs.

FIG. 3. E. K. K. Roentgenogram of chest January 30, 1935. Note moderate fibrosis at hila; lungs otherwise clear.

FIG. 4. E. K. K. Roentgenogram of chest May 1, 1935. Note increase in hilar shadows, mass in right upper mediastinum, and soft infiltration in right upper lobe.

amination the rectal temperature was 101° but, aside from an extensive stomatitis from which smears revealed Vincent's spirilla in abundance, no abnormalities were discovered. There was moderate secondary anaemia. The lungs were clear roentgenographically. (Figure 1.) The blood-Wassermann reaction was positive, but the cerebrospinal fluid was normal. The patient was given

two small doses of neoarsphenamine; the Vincent's stomatitis cleared up; and she was discharged from the wards on September 17, 1932, with a diagnosis of Vincent's stomatitis and latent syphilis.

In the Venereal Disease Clinic of the Baltimore City Health Department, to which she was referred for antisyphilitic treatment, she was given 8 doses of arsphenamine, each of 0.3 gm., at weekly intervals, followed by 8 doses of 0.2 gm. bismuth salicylate suspension in oil, during which she continued to lose weight and to complain of fatigability. After the first dose of the second course of arsphenamine, she became nauseated, vomited, and felt "weak and run down"; two more doses were given (each 0.3 gm.), and after the third she developed a productive cough and felt drowsy. She was readmitted to the Johns Hopkins Hospital May 1, 1933, seven months after her first admission, drowsy, semistuporous, and obviously very ill. The rectal temperature was 104.4°, the pulse 132, and the respirations 28. The mucous membranes were cyanotic, and there was oral sepsis, but no Vincent's organisms were found in smears. Examination of the lungs was unsatisfactory because of her condition, but there was obviously an extensive infiltrative process throughout both lungs, and roentgenogram (figure 2) revealed an extensive seeding infiltration of the upper half of both lungs. The remainder of the examination was negative, except for moderate secondary anaemia. The cerebrospinal fluid contained 104 cells per cmm., 62 per cent of which were lymphocytes, and there was a pellicle-formation, but no tubercle bacilli could be found. The next day she developed opisthotonus, a positive Kernig sign, and positive Oppenheim and Gordon signs on the left. On May 4, the cerebrospinal fluid contained 204 cells per cmm., 92 per cent of which were lymphocytes, and tubercle bacilli were found. Death occurred on May 6, 1932. Autopsy revealed an extensive bilateral apical pulmonary tuberculosis, tuberculous meningitis, and scattered miliary tubercles throughout the viscera.

*Case 15:* E. K. K., 49,965. This colored girl of 16 was seen in the Syphilis Clinic of the Johns Hopkins Hospital January 30, 1935, complaining of labial sores of three weeks' duration. Her past history revealed that she had always been susceptible to colds, tired very easily, had gained no weight for two years, and two years before had had an attack of pleurisy. There was a questionable history of a small haemoptysis one year before. Upon examination she was undernourished, presented typical *condylomata lata* on the labia, but otherwise no abnormalities were discovered. Roentgenogram of the chest (figure 3) was normal.

She was given 5 doses of 0.3 gm. arsphenamine at weekly intervals, but complained that the drug made her feel very badly. Treatment was therefore continued with 3 doses of neoarsphenamine, 0.6 gm., followed by 5 doses of bismuth salicylate, 0.2 gm.

On May 1, three months after the start of treatment, she returned, complaining of pain in the chest, fever, and productive cough of two weeks' duration. Examination revealed a temperature of 100.4° (rectal) and there were signs of changes in both lungs. The roentgenogram (figure 4) revealed a bilateral increase in the hilar shadows, a mass in the upper right mediastinum, and an area of soft infiltration in the right upper lobe.

She is under observation; it is too soon to offer an opinion regarding prognosis.

Since these 15 cases have occurred among approximately 20,000 patients treated, about 70 per cent of whom were negroes, one may raise the question as to whether equally as many instances of fulminating tuberculosis might not have been observed in an equally large number of patients not affected by syphilis or by treatment for it. Although our clinical impression leads us to believe that in these patients there was a cause-and-effect relationship between intensive arsphenamine therapy and the acute onset of tuberculosis, we cannot feel that the point is proved. Furthermore, we regard it as unlikely that it can be definitely proved on the ground of clinical experience alone, and that it is desirable that animal experimentation be undertaken to settle the issue.

## SUMMARY

1. Divergent opinions have been expressed concerning the incidence of coexistence of tuberculosis and syphilis. The difficulties in accurately determining this incidence are indicated; it is pointed out that no study which is beyond criticism has been made of the question, and the conditions to be fulfilled before conclusions may be reached as to a positive or negative correlation in incidence of the two diseases are detailed.

2. There are no clinical data upon which to determine the effect of tuberculosis upon syphilitic infections; such information must come from animal experiments, which, by their nature, are difficult to evaluate in terms of human disease.

3. Previous considerations of the effect of syphilis upon tuberculous infections have often neglected to include an evaluation of the effects of antisyphilitic therapy. There is evidence, however, that untreated syphilis affects adversely the course of pulmonary tuberculosis.

4. Mild antisyphilitic therapy is of benefit to patients with syphilis and tuberculosis, as judged by the signs of tuberculous activity in comparison to patients with both diseases whose syphilis is untreated.

5. Current practice in the treatment of syphilis in tuberculous patients is detailed, and is criticized because it is based upon the assumption that tuberculosis is always the more important disease.

6. The suggestion is made that the two diseases coexisting may be treated properly only by the close coöperation of experts in both fields.

7. A group of 15 cases is presented in which the administration of intensive antisyphilitic therapy was followed by the development of a previously unrecognized (and we believe, unrecognizable) pulmonary tuberculosis with rapidly fatal results. Two of the cases are presented in more detail, as being typical of the group.

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# THE PROBLEM OF COEXISTING SYPHILIS AND TUBERCULOSIS IN THE LIGHT OF CURRENT OPINION AND PRACTICE

C. St.C. GUILD[1] AND MARION NELSON[2]

Syphilis and tuberculosis are found to exist in the same patient with sufficient frequency to warrant study of this phenomenon. This is not surprising in view of the fact that both are chronic diseases widely distributed throughout the population. What is surprising, however, is the wide diversity of opinion as to (1) whether or not the presence of syphilis adversely affects the tuberculosis patient's chance of recovery; (2) whether or not, in the presence of tuberculosis, syphilis should be treated; and, if so, (3) what drug or drugs should be used and in what dosage.

An analysis of all the literature on these points would be extremely interesting if somewhat bewildering, but to illustrate how opinions diverge on the first point, it should suffice that we quote from two recent and authoritative books on syphilis.

"These two chronic infectious processes," say Schamberg and Wright (1), "act adversely upon each other as would be expected."

"The association of tuberculosis and syphilis," says Moore (2), "seems in some intangible manner to be of favorable import or at least not markedly unfavorable for each disease. This relationship may be markedly disturbed by treatment."

In view of the high incidence of both these diseases in the Negro, the National Tuberculosis Association's *Committee on Tuberculosis among Negroes* became keenly interested in this problem and, after some preliminary data had been gathered, it was decided that the present status of opinion and practice in a number of our larger sanatoria should be investigated. With the assistance of Dr. Walter Clarke of the American Social Hygiene Association and Miss Jessamine S. Whitney, Statistician of the National Tuberculosis Association, a brief questionnaire was pre-

[1] Secretary, Committee on Tuberculosis among Negroes, The National Tuberculosis Association.

[2] Statistical Assistant, The National Tuberculosis Association.

pared and sent to the medical directors of 96 large sanatoria (including state, county, municipal, and private institutions) in some 35 different states. The response was unusually good, since, without follow-up, 67 institutions submitted information giving accurate data as to the incidence of syphilis in some 25,000 tuberculosis patients and an excellent cross-section of current practice in dealing with coexisting syphilis and tuberculosis.

*The incidence of syphilis in tuberculosis patients:* Half of the institutions reporting a routine test use both the Wassermann and Kahn methods. Ten use the Wassermann only, and seven the Kahn only. Five report the use of the Wassermann plus one other test, such as the Kline or Hinton, and four use three tests on each patient. In only one instance was one of the other tests used to the complete exclusion of the better known Wassermann or Kahn.

In the following discussion we are assuming that the Wassermann or Kahn test is a reliable index as to the presence of syphilis.

Of the 54 institutions making a routine blood-test on all patients admitted, 50 gave complete information as to the number admitted and the number giving a positive blood-test classified according to color and sex. These institutions admitted during the year, 1933, a total of 20,281 patients, of whom 17,348 were white and 2,933 colored.

Of this entire group, 1,328 patients, or 6.5 per cent, gave a positive blood-test for syphilis. In the white patients, 4.1. per cent had positive blood-tests as against 21.0 per cent in the colored.

In the light of these figures it is interesting to note what happened in those 12 institutions where no routine test was made but where complete data as to the number of patients admitted and the number giving a positive blood-test are available. In these institutions a blood-test is made "in all suspicious cases," "only in cases where the patient requests such a test," "every case in which the sputum is negative," etc. Here we have an entirely different picture. These institutions admitted during 1933 a total of 4,802 patients (4,621 white and 181 colored) and a positive blood-test was obtained in only 1.4 per cent of these patients (white, 1.2 per cent; colored, 5.5 per cent).

The foregoing figures appear to justify two important conclusions: (1) they indicate that where no routine blood-test is made and such test is performed only on some special indication, approximately three out of every four cases of syphilis are missed; (2) they shed some additional

light on the tenability of the theory expressed by Marino and Fournier (3) and others that syphilis predisposes to tuberculosis. If this be so then it would be logical to expect that in this large and representative group of tuberculosis patients we should find that the incidence of syphilis would be significantly higher than in the general population.

Our figures have been discussed with the American Social Hygiene Association, and in their opinion the incidence of syphilis in this large group of the tuberculous is what one would expect to find in groups of similar age and color distribution in the general population. While more detailed analysis should be made, these figures suggest that syphilis does not predispose to tuberculosis.

*The effect of coexisting syphilis on the prognosis of tuberculosis patients:* Chadwick (4) states that the presence of syphilis lessens the patient's chances of recovery from tuberculosis. According to his figures the incidence of progressive tuberculosis in white patients is more than twice as high (110 per cent) and in colored patients more than 50 per cent (54 per cent) higher, when the Kahn test is positive on admission.

Among the medical superintendents who expressed themselves on this point opinion was about evenly divided. Half of those reporting were of the belief that syphilis had little or no effect on the tuberculosis prognosis, and the other half that the presence of syphilis definitely affected the tuberculosis prognosis adversely.

*The treatment of syphilis in the tuberculous: to treat or not to treat:* On this subject there is a wide divergence of opinion, the weight of which seems to be that some form of antisyphilitic treatment should be given, but a few maintain that it is best to disregard the syphilis unless it be causing clinical symptoms or, as one of them puts it, "We do not treat a positive Wassermann." While some are of the opinion that the tuberculous process would improve little, if any, unless the syphilis is vigorously attacked, the experience of others is that antisyphilitic treatment too often aggravates the tuberculosis and that practically all the treatments now employed in dealing with syphilis are harmful to pulmonary tuberculosis.

As to the actual practices of these institutions in the treatment of their syphilitic patients, it was found that antisyphilitic treatment was given to 64 per cent of the patients with positive serological reactions for syphilis in institutions making a routine blood-test, and to 60 per cent of such

patients in institutions in which no routine test was made. It is evident then that approximately one-third of those patients in whom both syphilis and tuberculosis exist receive no antisyphilitic treatment whatever.

*The choice of medication and dosage:* Of the 55 institutions answering this question, 42 report the use of both the arsenicals and the heavy metals, 7 use neoarsphenamine only, and 6 nothing but the heavy metals. One institution reported the occasional use of potassium iodide in addition to neoarsphenamine and thiobismol, but stated that its use was limited to cases of syphilis of the central nervous system.

No comparison of the dosage in which the heavy metals are used was possible as so many different preparations were listed. With the arsenicals, however, it is possible to indicate the wide range of dosage in which neoarsphenamine, the preparation most frequently used, is given.

*The use of neoarsphenamine according to dosage*

| DOSAGE | NUMBER OF INSTITUTIONS |
|---|---|
| *grams* | |
| 0.2 –0.4 | 10 |
| 0.45–0.6 | 16 |
| 0.9 | 1 |

It is evident that 10 of these institutions are using small doses, 16 of them doses which may be classed as of average size, and one a very high dosage. It should be stated that with very few exceptions the interval between treatments was given as one week. As to the number of doses given, there is so little uniformity that it is impossible to fit the information to any well defined classification.

## SUMMARY

1. Data on 20,281 tuberculosis patients (17,348 white; 2,933 colored), on whom routine blood-tests were made, indicate that 4.1 per cent of the white and 21.0 per cent of the colored patients gave a positive Wassermann and Kahn reaction.

2. Those institutions that make a blood-test only because of some special indication or at the request of the patient miss three out of every four cases of syphilis (syphilitic infection).

3. Since the incidence of syphilis in this group is not significantly higher than one would expect to find in similar color- and age-groups in the

general population, our evidence suggests that syphilis does not predispose to tuberculosis.

4. One-third of all tuberculosis patients who have syphilis receive no antisyphilitic treatment whatever.

5. While in most sanatoria both the arsenicals and the heavy metals are used in the treatment of syphilis, a few use nothing but the arsenicals, and others nothing but the heavy metals.

6. Only in the use of neoarsphenamine was it possible to indicate the divergence of opinion as to the proper dosage. Here we find 10 institutions using a fractional dose, 16 a dose of average size, and one an amount considered high for routine administration even in a nontuberculous patient.

## CONCLUSIONS

While it is recognized that there can be no hard-and-fast rule, it does appear that sufficient study could bring about more uniform procedures, and it is hoped that the sanatoria, for which these questions are extremely important, will make further investigations.

It seems reasonable to expect that a study of a large number of case-records will confirm or disprove Chadwick's opinion that syphilis lowers a patient's resistance to tuberculosis, or that careful observation of a large series of cases would finally answer the question as to whether or not the coexisting syphilis should be treated. If so, the next step would be to determine the drug or drugs of choice under different circumstances and their optimum dosages.

These are important questions, particularly to our sanatoria, and the American Sanatorium Association might well attempt, as one of its objectives, the solution of at least one phase of this problem.

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# FIRST STEPS IN PNEUMOLYSIS[1]

C. H. ANDREWS

Closed intrapleural pneumolysis, introduced by Jacobaeus of Stockholm in 1913, is now in an established position as a valuable aid in the collapse treatment of pulmonary tuberculosis. Along with artificial pneumothorax, phrenic-nerve interruption, and thoracoplasty, the cutting of pleural adhesions must be available when indicated if the best is to be secured from a program of collapse therapy.

While many sanatoria and tuberculosis clinics are not equipped, as yet, to do this work, it was thought that a record of the experience of introducing the procedure in the group of three sanatoria operated by the Saskatchewan Anti-Tuberculosis League would be of interest.

All pneumothorax workers are familiar with the high percentage of cases in which adhesions prevent satisfactory therapeutic collapse. In a substantial proportion of these cases this can be secured by severing the adhesions.

Closed intrapleural pneumolysis, as may seem unnecessary to state, consists of introducing, under local anaesthesia, two cannulae into the pneumothorax space, inserting an electrically lighted thoracoscope through one opening and a cutting instrument, either cautery or electrosurgical, through the other. Then, under visual control, the adhesion is severed by one or the other of these "bloodless" methods. The details of the technique need not be given here. They can readily be found in numerous articles in the literature of tuberculosis and thoracic surgery. Judging from perusal of a preliminary draft, Matson's section in Graham, Singer and Ballon's *Surgical Diseases of the Chest*, recently issued by Lea & Febiger, is the most comprehensive treatise on the subject yet published.

While this closed intrapleural or internal operation by puncture of the chest-wall appears to be the one of choice, it is interesting to note that in some quarters the previously discarded method of external operation

[1] From the Prince Albert Sanatorium of the Saskatchewan Anti-Tuberculosis League, Prince Albert, Saskatchewan.

through an open incision in the chest-wall has been revived with improved technique and very satisfactory results.

Our first contact with internal pneumolysis, other than through the literature, was in the winter of 1930–1931 at the City of London Hospital for Diseases of the Heart and Lungs, Victoria Park. Here were observed several operations performed by Dr. F. G. Chandler, who was extremely kind in demonstrating his technique and furnishing a great deal of information regarding the problems involved. This internist asserted that the procedure need not be left to the thoracic surgeon but could be carried out quite satisfactorily by physicians familiar with tuberculosis and artificial pneumothorax.

On returning from England, an opportunity occurred to visit Dr. Ralph C. Matson of Portland, Oregon, who has done much to popularize the operation on this continent. This thoracic surgeon was very kind in demonstrating his equipment and discussing the procedure. Unfortunately, no operative work was done during the short stay in Portland. Dr. Matson also offered encouragement to attempt the work.

After this visit the decision was made to get Matson's instruments and an electrosurgical unit made on this side of the Atlantic. The greater difficulty in obtaining service and replacements weighed rather heavily in the decision against the English equipment, which is excellently made and has some points in its favor, as, for example, it can be sterilized by boiling as Matson's cannot.

For the actual cutting two means are available,—the original cautery of Jacobaeus, and the electrosurgical method introduced, we believe, by Matson. The latter technique is considered by most operators to be the safer and permits of more extensive work being done as the operator's experience and expertness increase. However, quite extensive folds have been severed successfully with the "cold" cautery, and some who have both available prefer this method for string and small cord adhesions. Maurer, in Switzerland, combines the two, coagulating first and then cutting with the electrocautery.

The relative cost of the equipment necessary for these two methods has considerable to do with the decision of which to use. A cautery set can be obtained for about $200.00, while the electrosurgical equipment with one thoracoscope and necessary accessories costs $700.00 or more, depending principally on the surgical diathermy unit included.

Fortunately the way was opened to install the latter and the following items were secured: Matson's trocar and bakelite cannulae, and elec-

trodes (made by McKissick, Portland), Jacobaeus-Unverricht indirect 90°-vision thoracoscope (Wolf), Bethune's transilluminator (Pilling), a formalin vapor sterilizer and a portable surgical diathermy apparatus (Mobile Bovie unit, Liebel-Flarsheim) capable of giving suitable coagulating and cutting currents. Later it is hoped to add a Kremer direct-vision telescope, and an intrathoracic haemostat with insulated shaft, which may be inserted through the cannula and connected with the diathermy unit for coagulating tissue within the instrument's jaws. All this equipment is readily shipped from one institution to another.

The bakelite cannulae have an advantage over metal ones, either rigid or flexible, in that they furnish additional insulation, practically removing the possibility of a short circuit to the chest-wall with resulting burns. They, however, do not permit the use of an electrode with a curved shaft such as is included in most sets, but one of Matson's electrodes may be curved and another angled after insertion through the cannula, by turning a fluted segment of the handle, thus giving the advantages of both the straight and curved instruments. These electrodes have extensions which may be fitted between the shaft and point, and are supplied with ball, needle, and blade tips which are interchangeable.

What is considered a minor improvement to this adjustable curve electrode was made by continuing down to the tip the white line on the handle which indicates the direction of curve. By seeing this line as the instrument is being manipulated within the chest, the operator, without removing his eye from the thoracoscope, is assured of the direction the tip will move and of the plane the curve to be formed in the shaft will take. The adjustable angle instrument, while somewhat more convenient to use, has the disadvantage that its joint is not insulated. This makes it necessary for the operator ever to be on the alert to see that this joint is not in contact with tissue when the current is flowing. Such contact might easily result in serious damage being done.

The Jacobaeus-Unverricht indirect thoracoscope with the line of vision at right angles to the shaft was selected as giving the best visual field and being the most useful all-around instrument if only one was to be used. In observing work being done elsewhere with the direct-vision telescope alone, it appeared that to secure suitable intrathoracic relations of the optical and cutting instruments to each other and to the adhesions, especially to those at the more common sites, it was necessary to place the two cannulae and instruments in positions that seemed to be very awkward for the operator. Consequently the subsequent manipulations

were more difficult. However, the direct instrument is more convenient in some cases; having both is preferable.

It appeared that there was a defect in the usual technique in that the eyepiece of the thoracoscope and the fingers holding it easily came in contact with the operator's eyebrow, an unsterile area. This defect was overcome by the wearing of sterilized large-lens glasses and a mask which covered the entire face except for a narrow horizontal slit across the eyes. Chance contact is thus prevented. No evidence is offered that this precaution is necessary.

The transilluminator devised by Dr. Norman Bethune of Montreal has proved to be very useful. While having a curved shaft the diameter is so small that it can be used through Matson's straight bakelite cannulae. By placing a light behind an adhesion and observing with the unlighted thoracoscope it is possible to get a much better idea of its thickness and whether or not it contains blood-vessels or lung tissue than can be obtained with the thoracoscope alone. Current for both the transilluminator and the thoracoscope is obtained from an adjustable two-cell battery unit of flash-light size (Boehm).

The formalin vapor sterilizer, such as is used for catheters and urological instruments, was included, as the electrodes and optical unit cannot be boiled. The time required to carry out this method of sterilization is a disadvantage, especially when doing work in different institutions. Only two operations can be performed a day, one in the early morning and one in the late afternoon or evening.

Various standard surgical diathermy units have been used for adhesion cutting and have been reported as satisfactory. Apparently any good one will do, provided the high-frequency current delivered is not a pure cutting current, that is, continous and undamped. Matson urges the use of the Davis-Bovie instrument on account of the variable damping feature obtainable with this machine. With this a cutting current of any selected strength may be damped at three different settings, thus incorporating light, medium, or heavy degrees of coagulating power with the cutting current for the simultaneous dehydration and sealing of the tissue at the edges as the cut is being made. Our small mobile Bovie unit does not have this desirable feature, but delivers a cutting current somewhat damped, resulting in moderate concurrent haemostatic action.

It seems impractical to have the operator control the machine when so many other things are demanding his attention at the time. Notwithstanding the sterilizable handles supplied on many machines for current

selection and power control, it is better to have a technician present for this purpose, and a foot-switch, preferably with a single treadle, for the operator is an almost necessary accessory. A small shaded desk-light under the technician's control is convenient, and gives sufficient illumination when any is required in the dark operating room.

The various operating thoracoscopes with which the operation is done through one hole in the chest were not considered. Most authorities agree that the patient tolerates two punctures as well as one, and the two-hole method, using straight cannulae, has the added advantage that the instruments may be interchanged in the cannulae, which often gives a better view or easier access to an adhesion than that secured at first. These complicated combined viewing and operating instruments appear to be used more extensively by their inventors than by others.

Anaesthetizing the costal attachment of the adhesion before cutting is another point where practice and equipment differs. At Victoria Park, London, this is done almost routinely through the cannulae with an especially designed long needle adapter or a direct-vision telescope which delivers the local anaesthetic through a needle at its tip. On the other hand, Matson states that he has never felt any need for this anaesthesia. In some quarters it is secured by externally blocking the nerves to the area in the intercostal spaces near the vertebrae. Neither method has been used here and pain has not been a troublesome feature.

One more point regarding equipment. There does not appear much need for having instruments which make an air-tight fit with the cannulae. With Matson's set there is free communication between the pleural space and the atmospheric air throughout the operation. No ill effects have been observed from this even in patients with mediastinal herniae, and in those with contralateral pneumothorax. The completely closed technique attempting to maintain the existing intrathoracic pressure does not appear necessary, and the inability to increase pressure during the operation has not been a disadvantage. Smoke produced by cutting has given no trouble and its removal has not been needed.

After securing the equipment the next step was to become familiar with the coagulating and cutting currents produced by the electrosurgical unit. This was done first on meat and then on anaesthetized animals. The effect of currents of different strengths, on different tissues, with the ball, point, and blade electrodes, and with these being moved at different speeds, was studied.

At the same time, practice of the bimanual manipulation of the

thoracoscope and electrode was being carried on. This was done on a dummy chest constructed on a skeleton. A cardboard partition was fixed in place to represent the mediastinum. Hooks were placed on this at the approximate position of the lung roots, and elastic bands were stretched from these to various parts of the thoracic cage to represent adhesions. The thorax was covered with ¼-inch felt, closely fitted and sewn in place. A diaphragm of felt was also fastened in position. With the felt over the ribs the cannulae were held in place very much as in the living subject. Invaluable practice was obtained in orientation within the thorax with the 90°-vision instrument from various points of entry.

Even more helpful was the development of ability to place the tip of the electrode quickly and surely where it was wanted while guiding it under thoracoscopic vision. It took considerable practice at this to become reasonably expert. The chief difficulty lies in the fact that the line of vision is at right angles to the direction in which the operator is looking, and the electrode must be moved by the hand in a different direction than that which appears to the eye to be the right one.

This form of dummy chest would seem to furnish as good, if not better, practice than the elaborate ones supplied by instrument makers. The advantage of stringing within a dummy chest strips of meat to represent adhesions is not apparent if the cutting experience is obtained on meat and animals and the manipulative technique is developed on the dummy.

With this background operative work was essayed. To date, operations have been attempted on 22 patients. As yet the one operator is doing the work in all three sanatoria.

The results have been very satisfactory, about 60 per cent having been clinically successful. In several, the operation resulted in obliteration of large cavities which had shown no tendency to close under pneumothorax. In two of them the two-stage procedure was carried out. In this, at the first operation, an adhesion too large and short to cut safely was encircled near its costal attachment by a zone of coagulation and was found some weeks later to be stretched out into a relatively thin band which was easily cut.

In several cases what appeared to be strings on the X-ray films turned out to be the edges of broad spool or fold adhesions too large to cut. This bears out the statement of most writers that adhesions are usually more numerous and extensive and the operation more difficult than the preliminary X-ray study suggests. In some of the attempted cases no benefit was derived by the patient; what cutting it was thought could be

done safely did not free the lung. Probably, with more experience and less timidity on the operator's part, more of this group could have been successfully operated upon.

The occurrence of operative and postoperative complications has not been unduly frequent. Subcutaneous emphysema was quite extensive in three of the early cases. Several developed effusion which followed the usual benign course of fluid complicating artificial pneumothorax. In one case an existing effusion became a sterile empyema. Haemorrhage from the costal stump was encountered twice but was readily controlled by deep coagulation. One patient with extensive disease (a large cavity and bilateral pneumothorax) developed, shortly afterward, an acute spread on the opposite side; possibly this should be attributed to the operation.

The series of cases has been small as a very conservative attitude has been adopted in accepting indications for operation. It was considered that adhesions should be holding diseased areas uncollapsed or cavities open and the patient have a positive sputum before cutting should be attempted. Also, reasonable hope should exist that the adhesion could be safely cut and the operation result in a therapeutic collapse being obtained. Often the former point can only be settled after the thoracoscopic study.

Operation has not been attempted in all cases presenting apparently cutable adhesions on the X-ray film. The argument is used that any resulting increase in collapse ensures a more solid fibrosis and a safer healed lesion in the end. This may be so, but, as yet, adhesions without the foregoing definite indications for cutting have been left alone, no matter how inviting they appeared to the operator.

Without minimizing the difficulties and dangers involved, closed intrapleural pneumolysis appears to be an operative procedure well within the abilities of most physicians working in tuberculosis. It is difficult to see where experience in general surgery, or even thoracic surgery, would be of much help, as the technique of this work is so radically different. Familiarity with using the cystoscope with its similiar indirect field of vision would be of some assistance, and experience with electrosurgical technique would be valuable. Otherwise, a knowledge of pulmonary tuberculosis and pneumothorax therapy, a mechanical turn of mind, and good manual dexterity are the main requirements.

Developing this work without special training under an expert has been most interesting and instructive. The results have been a source of

satisfaction, with the institutional stay of some patients materially shortened, others saved from a deforming thoracoplasty, and possibly some from a down-hill course. And, in the organization that gives free treatment to all the tuberculous residents of the province, the cost of equipment has already been repaid in decreased treatment days and in removing the necessity for more expensive surgical work.

This article presents little that is new, but a compilation of the information herein would have obviated months of delay and have been a great help to us in taking our first steps. It is hoped that the account of the experience of one organization in inaugurating the use of this necessary adjunct to collapse treatment will be of assistance to others who may be planning to become equipped and undertake the work.

Our thanks are due to the men mentioned and to others, masters of the art, for information and advice so readily given; and to Dr. R. G. Ferguson, Director of Medical Services of the League, for his encouragement and for securing the necessary equipment.

# RESULTS IN INTRAPLEURAL PNEUMOLYSIS[1]

LEROY S. PETERS AND P. G. CORNISH

After having treated tuberculosis by means of artificial pneumothorax for twenty-three years, one is permitted to view the method in retrospect, and this, let it be said, to one's advantage.

In the early years, many patients were not considered safe for compression treatment, but to-day the same patients would be given that advantage and be made well. With experience we grow braver and braver, and in the present era pneumothorax workers are found in every centre of population while in the beginning only health resorts found them available. To-day we can start a pneumothorax, and feel safe to let the patient wander far afield if necessity so dictates and know that he can be referred to a physician who can carry on the treatment.

In the beginning, probably not more than 5 per cent were considered safe risks, while now many institutions boast from 50 to 80 per cent, under some type of compression therapy. This high percentage can be safely handled in sanatoria where the patient is under careful supervision, but, in our opinion, it is not warranted in private practice. The odds are too much against a successful outcome. The physician who rushes in where angels fear to tread is carried away by the brilliant effects when treatment is instituted. But, if he follows up carefully the end-results in private practice, his enthusiasm will be dampened by the growing number of failures.

In other words, when long chances are to be taken, institutional care should be obligatory.

Do not let us be misunderstood by the foregoing statements. We doubt if there are more enthusiastic believers in compression therapy than ourselves in the entire country, but this enthusiasm must be tempered with common-sense. There is too much optimism in the current literature, and too many men in small communities are becoming compression specialists overnight, depending on an occasional tuberculosis patient to provide the experience necessary to make their work successful.

[1] Presented at the thirtieth annual meeting of the American Sanatorium Association, Saranac Lake, New York, June 24, 1935.

We are convinced that the observation of seasoned workers in this field will bear us out in this statement.

All this is not said with the idea that patients must be treated only in sanatoria to be treated successfully. We are not here to raise the hopes of the medical director at the expense of the private practitioner. We realize that the great mass of tuberculous invalids could not be treated in institutions if they so desired. But we want to emphasize the fact that if we were patients we should feel much safer in the hands of a private practitioner who kept his percentages down rather than try to equal the 80 per cent that some sanatoria care for.

In our own work twenty-three years ago, pneumothorax was given to less than 5 per cent, but over the years this has increased, so that to-day some form of compression therapy is instituted in 30 per cent of patients.

Having relieved our minds of a few of the pin-pricks that irritate, we shall now come to a consideration of the subject of this paper.

A therapeutic pneumothorax to be successful must have effected cavity-closure and rendered the patient bacilli-free. Unless this has been accomplished it is a waste of the physician's time and the patient's money to drag out a partial collapse over months and years, hoping against hope that the days of miracles are not passed and that ultimately success will crown our efforts. A positive sputum is the tuberculous invalid's death sentence either by extension in the pulmonary area, or by the complication of a laryngeal or intestinal tuberculosis. All the optimism of the attending physician cannot change the picture.

The argument that adhesions may be stretched or broken has been made many times. And many times has the danger of this procedure been pointed out, both by discussion on the floor of medical meetings and in literature of compression therapy, yet the optimists go blithely on, forgetting that these same adhesions may be severed with little or no inconvenience to the patient and with far less serious complications.

It took years to educate the profession to the value of pneumothorax, and it is taking years to teach them the value of a satisfactory collapse. It is appalling how few pneumothorax workers are availing themselves of intrapleural pneumolysis, and yet here is a method that converts over 78 per cent of partial-collapse into complete-collapse cases, and turns failure into success for the patients.

Our work covers a period of seven years, during which time 244 patients were given an artificial pneumothorax. On 148, or 60+ per cent, a complete collapse was obtained, thus leaving 96, or 39+ per cent with only a partial collapse.

Of these 96, on thoracoscopy 8, or 9 per cent, were found not suitable for operation. The X-ray is not nearly as valuable in determining operative types as is direct exploration. Many times we will expect to find a burnable adhesion from the X-ray picture, only to be disappointed, and as often one will be surprised to find burnable adhesions that from an X-ray standpoint looked inoperable. In the final analysis, the X-ray's chief value is determining the site of approach.

Leaving out the 8 not burnable, we have 88 cases to consider. Of these, 69, or 78+ per cent, were converted into successful collapse with cavity closed; 8, or 9 per cent, showed clinical improvement; 5, or 6 per cent, no improvement; 6, or 7+ per cent, developed a natural pneumothorax; 24, or 27+ per cent, developed fluid; 2, or 2+ per cent, bled rather freely but the bleeding was controlled; and 1, or 1+ per cent, died the day of operation. Autopsy could not be obtained, but death was thought to have been due to embolism or possibly to a mechanical interference with the heart, since it was a left-sided case and a marked shift of the mediastinum occurred after the pneumolysis.

Since we have used the electrosurgical method the past three years, there is much less fluid-formation and bleeding is less apt to occur.

The 8 cases in which improvement occurred even without cavity-closure no doubt attained this through better compression of infiltrative areas around the cavity.

In all unimproved cases, or those not burnable, thoracoplasty was advised if the patient was a suitable risk.

In none of the eight showing improvement was the cavity closed by a continuation of the pneumothorax, and ultimately other forms of compression therapy were advised.

The percentage of natural pneumothorax cases seems high, but on analysis of the 6 cases it does not look so forbidding. The first patient operated on seven years ago, before experience had taught us better, from an X-ray standpoint looked suitable, but what we thought an adhesion proved to be the floor of a cavity. Cauterization was not completed when we discovered the mistake, but in a week's time a tear occurred with resulting empyema. This patient is alive to-day following thoracoplasty. Two others developed a natural pneumothorax two months after operation; so the pneumolysis cannot necessarily be blamed for this. The other three occurred within a week of the operation, and the pneumolysis can without question be blamed. This, however, reduces the percentage to 3.5.

Since using the electrosurgical method, the percentage of fluids has been cut to 5.5 per cent.

When one considers that 78 per cent of partial compression cases can be converted into complete collapse and thus made well, the wonder is that such a large number of pneumothorax workers are still reluctant to avail themselves of this added advantage in compression therapy.

*Summary*

244 cases under pneumothorax since pneumolysis was begun
96 cases of this number suitable for pneumolysis, or 39+ per cent
8 cases of the 96 found unsuitable after thoracoscopy, or 9+ per cent
88 cases to consider
69 of the 88, cavity closed, or 78+ per cent
8 of the 88, improvement, or 9+ per cent
5 of the 88, no improvement, or 6 per cent
6 of the 88, natural pneumothorax, or 7+ per cent
24 of the 88, fluid-formation, or 27+ per cent
2 of the 88, haemorrhage, or 2+ per cent
1 of the 88, operative death, or 1+ per cent

Since using the electrosurgical method, 36 cases with fluid-formation in 2, or 5.5 per cent.

# FIBRIN BODIES IN THE PLEURAL SPACE IN A CASE OF ARTIFICIAL PNEUMOTHORAX[1]

**With Necropsy**

WILLIAM A. ZAVOD

The purpose of this paper is to describe a case of artificial pneumothorax with fibrin bodies in the pleural space. Search of the literature reveals only 3 cases of fibrin bodies with autopsy records, none of them in the English language.

The first case was reported by Wischnowitzer (1). He described therapeutic pneumothorax on the right side complicated by a spread to the contralateral lung with fatal result. He found a fibrin body, the size of a chestnut, in the right pleural cavity. The body was caseous and histological study failed to reveal any cellular elements or *B. Tuberculosis*.

The second case was reported by Pomelzoff (2). His patient had a therapeutic pneumothorax on the left side for several years and roentgenograms showed the presence of fibrin bodies. Pneumothorax was induced on the right side because of the spread of the tuberculous process. Soon after the induction of the treatment the patient developed a tear in the right lung with an ensuing tension-pneumothorax, and died. Autopsy showed two fibrin bodies: one, the size of a hen's egg, was lying free in the pleural space; and the other, the size of a walnut, was fixed to the tissues. Pomelzoff studied these bodies chemically and histologically, and found their composition to be that of fibrin.

The third case was reported by Goljajew (3). His case came to autopsy nine days after a tuberculous pneumothorax, following which an effusion appeared. He found 14 small fibrin bodies of various shape, and ranging from 1 to 6 cm. in diameter. Histologically, they were composed of fibrin, in the meshes of which were partly degenerated cellular elements. Goljajew also found "seeds" in the centre of these bodies around which the layers of fibrin were deposited. Hager and Langebeckmann (4) saw a fibrin body *in vivo*, through a thoracoscope, and they described it as a smooth, glistening, umbilicated, ivory-colored mass, oval in shape.

[1] From the Tuberculosis Division, Grasslands Hospital, Valhalla, New York: Dr. John M. Nicklas, Chief of Service.

They also mention a personal communication from Dr. Thomsen, relating a fibrin body removed *in vivo* during an operation for empyema. The case was not reported. Bacmeister (18) mentions this case in his textbook as a rare phenomenon.

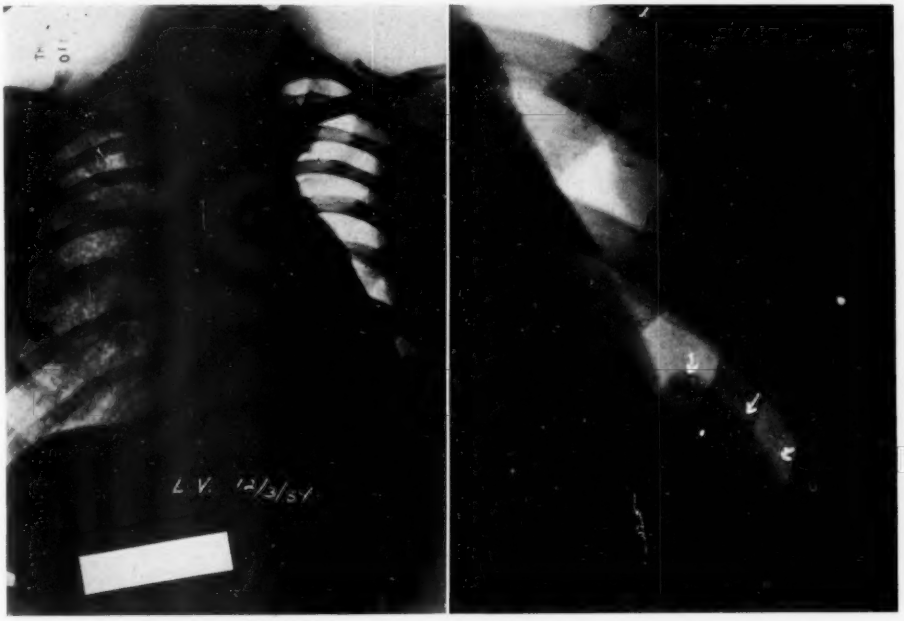


FIG. 1A FIG. 1B

FIG. 1A. Film, taken December 3, 1934, showing pneumothorax on left side and a fibrin body resting on the diaphragm. The fibrin body appears to be contiguous with the collapsed lung. The right side shows haematogenous dissemination of the tuberculous process.

FIG. 1B. Same film as figure 1A. Reproduction of the lower third of left chest (one-half natural size). Fibrin body is indicated by arrows.

### *Author's Case*

A white male patient, L. V., 44 years old, coal-miner by occupation. *Family* and *past history* irrelevant. Became ill with symptoms of respiratory disease in 1931. After some time tuberculosis diagnosed, and patient admitted to Tuberculosis Division of the Grasslands Hospital, July 29, 1932. *Diagnosis:* Far-advanced productive pulmonary tuberculosis. Process involved upper third of right lung and upper two-thirds of left, with cavitation in the latter. Sputum positive. Roentgenograms suggested old haematogenous seeding and pneumonoconiosis in addition to above clinical diagnosis. Therapeutic pneumothorax instituted on left side, August 13, 1932. A free pleural space was

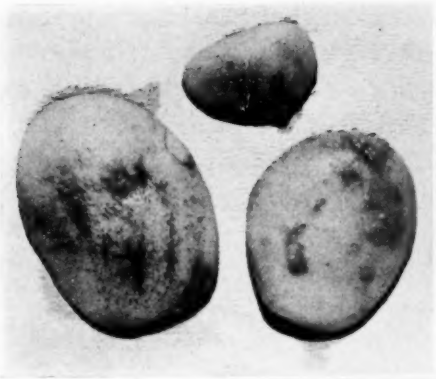

FIG. 2

FIG. 3

FIG. 4

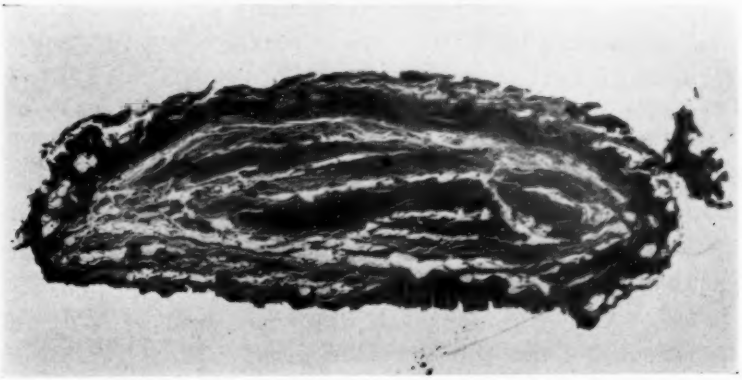

FIG. 5

FIG. 2. The three fibrin bodies as they appeared when removed from the left pleural space (one-half natural size). Umbilications are plainly visible.

FIG. 3. Collapsed left lung and fibrin body adherent to it as it appeared when removed from the chest. (One-quarter natural size.)

FIG. 4. Same as figure 3. After removal of fibrin body, showing bed and banked-up border apically. (One-quarter natural size.)

FIG. 5. Section of fibrin body, as seen with hand lens, showing concentric layers of fibrin. (Magnification, $\times 3\frac{1}{2}$.)

found and effective collapse resulted. Sputum negative in April, 1933. Fluid appeared in left pleural space, January, 1933, and laboratory examination of a specimen showed 3,840 white cells, no red blood cells, and no *B. tuberculosis* or other organisms on direct smear of centrifugated specimen. Patient discharged from hospital, November, 1933, as apparently arrested case, and continued his pneumothorax refills in Out-Patient Department. Fluid in left chest apparently had no ill effect on course of tuberculous process, and never rose high enough to warrant removal. In August, 1934, the fluid disappeared, when a mass, seen on the diaphragm in the left sulcus, was interpreted as a fibrin body (figures 1A and 1B). In December, 1934, three weeks after last refill, patient brought to clinic for examination because of slight fever, headache and dizziness. Examination revealed spread of tuberculous process over entire right lung, and symptoms of early meningitis; readmitted to hospital. The spinal fluid showed *B. tuberculosis* on direct smear. Patient failed rapidly and died December 12, 1934.

*Autopsy exerpts:* On opening the left hemithorax, the left lung was collapsed about 70 per cent and resembled a large spleen in size and appearance. Parietal and diaphragmatic pleurae covered with shaggy coat of fibrin. Three fibrin bodies found in pleural cavity (figure 2), two lying loosely on diaphragm posteriorly to heart and pericardium, and the third attached to base of lung in the anterolateral aspect (figure 3). The fibrin bodies measured $6\frac{1}{2}$ x 5 x $1\frac{1}{2}$ cm., 5 x $4\frac{1}{2}$ x $1\frac{1}{2}$ cm., and $3\frac{1}{2}$ x $2\frac{1}{2}$ x 2 cm., respectively. Their surfaces were smooth, glistening, and frequently umbilicated. They were ivory-colored, oval and flat in shape, resembling pebbles on a rocky seashore. Their consistency was that of a lipoma and they sank in water. The body attached to the lung was covered with a very fine translucent membrane that seemed to have a sparse blood-supply arising from the visceral pleura. When the fibrin body was detached from the lung, a bed was seen which was fairly smooth and showed a banked-up border apically (figure 4).

On section, the fibrin bodies were homogeneous and showed, with a hand-lens, lines suggesting laminae. Histological section displayed layers of fibrin (figure 5). No cellular constituents could be found, and preparations of sections with special stains were negative for *B. tuberculosis* and elastic fibres.

## DISCUSSION

Fibrin bodies are no rare phenomenon in active pneumothorax clinics, and are being encountered more often as pneumothorax is rapidly becoming so widely practised in tuberculosis. They were described in serous sacs by pathologists as far back as 1844. Rokitansky (5) found them in the pericardial sac following a serous pericarditis. Many pathol-

ogists after him have described fibrin bodies in the peritoneal cavity; but not until 1922 do we find any recorded evidence of them in the pleural cavity. Fleischner (6) was the first to describe a fibrin body that he saw on fluoroscopy in a case of therapeutic pneumothorax under treatment. There have been many recorded cases since then.

The most controversial point concerning them is their origin. Cellular proliferation of the pleura, preëxisting masses of false membrane, inflammatory products, conglomerations of fibrin from serous exudates in the pleural cavity, and haemorrhage into the pleural space have all been suggested. Of these the last two have the most proponents. The group of authors (1) (2) (6) (7) (8) (9) that advances the theory that fibrin bodies are formed by the agglomeration of fibrin in a pleural effusion bases its belief on necropsy findings and the lack of proof (in the cases they observed) that there was any exudation of blood into the pleural space at any time during the course of pneumothorax therapy. In this connection the case reported by Heacock and Van Ness (9) is of interest: their patient was a child, 3½ years old, nontuberculous, and ill with septicaemia complicated by spontaneous pneumothorax. A roentgenogram taken soon after the accident showed a partially collapsed lung, but no fluid-level in the pleural space. An exudate appeared three weeks later. After three months the fluid had been resorbed and a mass was seen on the diaphragm. It was freely movable and was pushed toward the apex as the lung reëxpanded. It eventually disappeared, the lung reëxpanded, and the child recovered. From the above citation it is evident that a source other than haemorrhage into the pleural cavity was the cause of the formation of the fibrin body. The spontaneous pneumothorax was not accompanied by haemorrhage, since the fluid level did not appear until three weeks after the accident.

The group of authors (10) (11) (12) (13) (14) (15), that advances the theory that fibrin bodies are of haemic origin, bases its belief on a few cases in which there was clinical evidence of haemorrhage into the pleural space following injury to an intercostal vessel during pneumothorax refills. Other writers (16) (4) do not commit themselves as to the origin of fibrin bodies. There is agreement, however, that fibrin bodies are of no known clinical importance, that they disappear spontaneously, and that the patient suffers no ill effects from their presence. Our own observations confirm these statements.

The size of fibrin bodies varies from that of a cherry to that of a lemon. They may persist roentgenographically from a few weeks to four years.

Their shape is usually flat and oval. They may be pedunculated, and lie loosely and freely movable or be adherent to the diaphragm, chest-wall or collapsed lung. They are white or ivory-colored, smooth and glistening, and often show many umbilicated superficial spots. The resemblance of the fibrin body in shape to that of a pebble may possibly be explained by the fact that the fluid in the pleural cavity has its rhythmic waves set up by the cardiac impulse, the rise and fall of the diaphragm, the movements of the chest-wall during respirations and changes in posture, not unlike the waves on a rocky seashore that impart a rolling motion to the fragments of rock, slowly grinding them to the smooth, flat, round or oval shape characteristic of a pebble.

The incidence of fibrin bodies in all cases of therapeutic pneumothorax is variously reported by different authors. Thus Sachs (12) found 2 cases in reviewing 700 cases with pneumothorax; Mende (17) observed three in 512 cases; and Hager and Langebeckmann (4), one in 400. We have 5 cases that show fibrin bodies roentgenographically among 226 patients receiving pneumothorax at present in the hospital and Out-Patient Department. We believe that the incidence is still higher, since a fibrin body may be blotted out by the heart-shadow and overlooked, unless the patient is carefully fluoroscoped from all angles. This point is well illustrated in the case described here, in which the roentgenogram showed only one body although actually three were found.

In most cases reported and in our 5 patients, the presence of effusion in the pleural space was noted for some time prior to the appearance of the fibrin bodies. Why they occur in some cases of pleural effusion and not in others is not known.

The diagnosis presents no difficulty. The bodies are readily seen under the fluoroscope or roentgenogram (when not obstructed by fluid or heart-shadow) as a sharply outlined dense shadow, frequently movable with change of the patient's position. Infrequently a conglomeration of fibrin may resemble an adhesion. We have seen one such case in which a pedunculated fibrin body arose from the collapsed lung and extended to the diaphragm. On fluoroscopy, however, the fibrin body swung like a pendulum, upon tilting the patient, and subsequent roentgenograms showed a gradual resorption of the band-like mass.

## SUMMARY

1. A case of therapeutic pneumothorax with fibrin bodies is described (necropsy).

2. The incidence of fibrin bodies during the course of therapeutic pneumothorax is greater than that reported until now.

3. The bodies are composed of fibrin, and are found in some cases of serous effusion rich in fibrin.

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# PRIMARY TUBERCULOSIS

## Observations among Tuberculosis Contacts[1]

MARK H. JORESS[2]

In the study of patients exhibiting the adult or reinfection type of tuberculosis, we are confronted with lesions generally consisting of infiltration and caseation, which, in many instances, result in liquefaction-necrosis and the production of cavities. Patients showing this type of pathological process are prone to develop toxaemias of varying degree and constitute the adult consumptives. Here, it is the pathological changes at hand which arrest our attention for the moment. Any elements present which denote obsolete lesions, the end-results of a primary infection, we look over hastily, since, from the standpoint of therapeutics, it is only the reinfection type of process which will engage our clinical attention.

In the same manner, when observing young patients who show evidence of a well-established tuberculosis of the juvenile variety, our attention is directed toward an evaluation of the pathological process as we find it. Here, too, we deal with the end-results of bacillary invasion. However, the lesions in this instance, contrary to the reinfection type of disease seen in the adult, constitute the end-results of the primary invasion, the so-called primary tuberculosis.

While searching for tuberculosis in the child's chest the clinician is in an advantageous position because he is able to observe the various phenomena which accompany the primary invasion. In the adult this is not possible because by the time adolescence is reached any preceding pathological change which may have been present following the first invasion has entirely disappeared. The manifestations of the initial or primary invasion precede by a variable but prolonged period the end-results of the primary infiltrate. The final picture of the latter is designated as *juvenile tuberculosis*.

It must be emphasized, however, that, in order to appreciate the

[1] From the Division of Tuberculosis, Boston Health Department, Dr. George T. O'Donnell, Director.

[2] Boston, Massachusetts.

various aspects of the primary and postprimary infection phenomena, it is of the utmost importance to study the child contact by means of serial roentgenography. It is the only accurate method which permits us to learn when the primary invasion has occurred, and to obtain a graphic picture of the various involutionary phases observed during the post-primary period. Above all, we are able to observe the formation of the end-results of the primary infiltrate, when classical juvenile tuberculosis becomes manifest.

In this article an attempt will be made to review some of the pathological, clinical and roentgenological phases of the subject, and describe several cases observed by the writer. In an analysis of these cases discussion will be limited to clinical-roentgenological observations.

The first publications to describe fully the evolution of the pathology of primary tuberculosis are those of Ghon (1) and Ranke (2). Ghon's thesis enunciated the concept that the primary tubercle is the end-result of the first invasion of the lungs with the tubercle bacillus. The tubercle named is seen on the radiograph as an isolated, calcified shadow, situated anywhere in the lungs, and is designated as the *obsolete tubercle*. The latter is the landmark denoting the place where the bacilli make their first inroads. The infection having been overcome, the surviving bacilli are imprisoned by the process of calcification, thus establishing the primary, or Ghon, tubercle.

Ranke carried the primary-invasion concept of Ghon still further and elucidated a second evolutionary stage. By focusing attention upon the lymphatic system of the invaded lung, he demonstrated that, aside from the initial focal reaction set up against the invading bacteria, there occurs a hyperactivity in the lymphatic channels, particularly the lymph nodes. In this lymph-node system is to be found the means for establishing and maintaining a defensive barrier against dissemination of bacilli from the point of entry to other parts of the lung.

The recognition of lymph nodes at the hilum of the lung with evidence of calcification within them is an implication that the evolution of the primary infiltrate is being completed. The primary *Affekt* with the regional lymph-node enlargement (*complex*) constitutes the end-results of pathological changes occurring in the lungs of those coming in contact with the tubercle bacillus for the first time.

In 1921 the term *epituberculosis* was introduced by Eliasberg and Neuland (3) to designate a certain form of lung infiltration, pneumonic in

character, observed in the radiographs of children exposed to open cases of tuberculosis. These children were obviously exhibiting the pathological process which resulted from a primary invasion with the Koch bacillus.

Although still used by some writers, the term *epituberculosis* has given way to a new terminology. Primary tuberculosis, better describing the nature of the process at hand, is the term most frequently employed at present, particularly in the American literature.

Numerous discussions on the subject of primary tuberculosis have appeared in various publications, especially with reference to the nature and character of its pathogenesis.

The first invasion with the tubercle bacillus, and the accompanying cellular response exhibited by the virgin lung have been worked out by Krause (4). He has described it as the initial phenomenon occurring in the course of the evolution of the primary infection. In his thesis Krause has indicated that the patch of pneumonic shadow appearing in a person exposed to the tubercle bacillus for the first time constitutes a specific mechanism of cellular pathology. It is his belief that the latter is a cellular response on the part of the nonallergic host to the tuberculoprotein of the invading microörganism.

The primary infiltrate, though extensive in distribution, is, as a rule, not detected on physical examination. According to Watts (6), it is recognizable as an entity only with the aid of the roentgenogram. It appears as a shadow of homogeneous density, pneumonic in character, and when observed by means of serial radiographs is found to persist for many months and even years.

The end-results of the primary infiltrate consist of either the formation of strands of fibrous tissue, or the deposit of calcium or both, producing the characteristic primary *Affekt*. These observations have been corroborated by such a careful student of the subject as McPhedran (5).

While involution of the primary infiltrate is taking place, lymph-node calcification within the corresponding hilum is seen to develop, and constitutes confirmatory evidence for the diagnosis of a primary tuberculous lung invasion. The phenomenon of hilum lymph-node calcification accompanying evolution of the primary infiltrate has been noted repeatedly by Opie (7).

As regards the clinical manifestations accompanying a primary tuberculosis, it is to be emphasized that they are, as a rule, of a mild nature. Rarely does the patient present symptoms of an acute illness. Moreover,

the great majority of cases detected with the aid of the X-rays would be overlooked clinically were it not for diligent search exercised in the examination of children exposed to open tuberculosis.

It is obvious that the child is well able to withstand the first infection. A working hypothesis to explain the patient's resistance may be offered on the basis of allergy. At the time of the first infection the child is in a state of anergy. Therefore, the soil may be considered as not yet sensitized to the tuberculoprotein of the invading microörganism. Contrasted with the nonallergic state, we find a rather marked allergic response among adults exhibiting the reinfection type of tuberculosis. The latter seem to lack resistance apparently because they have been sensitized as the result of a primary infection sustained early in life.

Thus we note that, while the lesions developing following reinfections frequently lead to rapid disintegration of the lung infiltrate, inducing manifestations of toxaemia with cavity-formation, the lesions of primary tuberculosis are characterized by a slow evolution, and clinical manifestations are generally mild, or are absent altogether.

A distinguishing characteristic of the primary infiltrate is its chronicity. Similar pneumonic shadows, like those caused by the pneumonococcus, last a short time and disappear by means of complete resolution. As stated, the shadows of primary tuberculosis persist for a long time, and when they finally disappear pathogenic evidence of their involution will be found in the production of fibrosis, calcification, or both. Some of the cases observed by the writer presented infiltrates lasting over a period of years.

The majority of children appear to handle the primary infection very well. In a recent publication Stewart (8) presents clinical studies on primary tuberculosis in which he often noted a total absence of clinical reaction. Even massive infiltrates were seen by him to provoke no marked symptomatic response. Other observers, as well, point to the relatively innocuous nature of the primary invasion with the tubercle bacillus.

The observations presented in this paper are based upon a combined clinical-roentgenological study of a number of children exposed to open cases of tuberculosis in their homes. First-hand knowledge of these cases was made possible through the writer's association as visiting physician to the tuberculosis clinics of the Boston Health Department. The routine examination of the contacts observed included history-taking, tuberculin-testing, physical examination and X-ray study in each in-

stance. The clinical course and roentgen changes were observed at frequent intervals, depending upon the clinical picture and ready coöperation on the part of the child's parents.

A review of the material studied disclosed a number of interesting facts. Evaluation of symptoms and careful physical examination failed to disclose the presence of intrathoracic disease. X-rays, however, revealed unmistakable evidence of varying degrees of lung infiltration of a pneumonic character. In the light of subsequent studies by means of serial roentgenography, the shadows noted were in each instance consistent with the cellular proliferation of a primary tuberculous infiltrate.

The cases observed were examined at frequent intervals. In a number of them the pneumonic shadow was seen to last as long as four years. The character of the shadow produced by the infiltrate was identical in every case. It was observed in nearly every portion of the lung field. With the exception of one instance, namely, that of a Negro child with a primary tuberculosis of the miliary variety, none of the cases presented the picture of an acute illness. What was noteworthy was the fact that symptoms referable to the respiratory tract were entirely absent, the exceptional case being that of the Negro child, which exhibited a considerable degree of dyspnoea over a long period of time.

The observations of McPhedran relative to the end-results of these infiltrates were borne out in this study. At some time in their evolution there occurred a proliferation of fibrous tissue or a deposit of calcium at the site of the infiltrate. In addition, lymph-node calcification at the lung root was observed at some time during the evolution of the infiltrate.

## DISCUSSION

In the course of search for tuberculous disease among the young exposed to open cases of tuberculosis, a number of them are found exhibiting parenchymal infiltrates, pneumonic in character. The pathological nature of the aforementioned infiltrates consists of a cellular proliferation constituting the focal reaction to the invading mycobacterium, and characterized by a total absence of signs of tissue destruction.

The diagnosis of primary tuberculosis is based upon the development and persistence of pneumonic shadows of marked chronicity. They are entirely devoid of stethacoustic findings so peculiar to pneumonic infiltrates caused by other bacteria. Patients with primary tuberculosis are generally lacking in symptoms referable to the respiratory system. Especially do they lack manifestations denoting clinical disability.

Contrasted with lung pathological changes denoting the adult or reinfection type of tuberculosis generally accompanied by toxaemia, with lung destruction, lesions of primary tuberculosis are notorious for their lack of toxic manifestations, and persistence of the infiltrate without undergoing destructive changes.

Primary tuberculosis can readily be overlooked in the child contact because of the usual lack of symptoms and physical signs. Its recognition is made possible through the use of serial roentgenography.

I am grateful to Dr. Cleaveland Floyd, Chief of Clinics, for permission to publish above data, and to Dr. H. F. R. Watts, Roentgenologist of Clinics, for the privilege to use his X-ray files.

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# BILATERAL APICAL NONTUBERCULOUS BRONCHIECTASIS

## Report of a Case

JOHN STEIDL[1] AND FRED H. HEISE[1]

Chronic lesions of the upper third of the lung are quite properly considered to establish a presumption of tuberculosis. When such lesions are bilateral the presumption is greatly strengthened. This paper reports a striking exception to this rule.

A female secretary of 28 was admitted to the Trudeau Sanatorium on November 28, 1933. At that time she had slight hoarseness, slight dyspnoea, cough, and expectoration of an ounce of purulent sputum a day. At first she dated her illness from catarrhal symptoms in 1922, but later admitted that she had had a cough since an attack of "whooping-cough" in infancy. In 1922, accompanying her usual cough and expectoration, she had several small haemoptyses of two or three drams. She also had sore throat and tonsillitis. Because of these symptoms a tonsillectomy was done. A chest X-ray was then taken and, because this showed some "trouble" with "activity" in the right lung, she was sent West where she stayed for eleven months, leading a fairly active life. During this time she had blood-spitting on one or two occasions, but her cough and expectoration improved somewhat.

On her return she began working as a secretary, and remained well until February, 1925, when she again had several small haemoptyses of one or two drams. She was allowed to continue working and was treated with tuberculin. In December, 1932, she had an acute illness with fever to 104°, general malaise and marked increase of cough and expectoration. After these symptoms subsided her cough and expectoration were worse than before and her sputum was blood-tinged. She was advised to rest, and artificial pneumothorax was discussed, but she continued to work until November, 1933, when, because of persistence of catarrhal symptoms and haemoptyses, she decided to come to Trudeau Sanatorium. During all this time her sputum had not been examined.

On admission to the Sanatorium her sputum was negative for tubercle bacilli, when concentrated, on eight occasions. The sputum was examined for elastic fibres twice and they were found once.

Chest X-rays showed mottling and string-like shadows in the upper two-

[1] Trudeau Sanatorium, Trudeau, New York.

FIG. 1

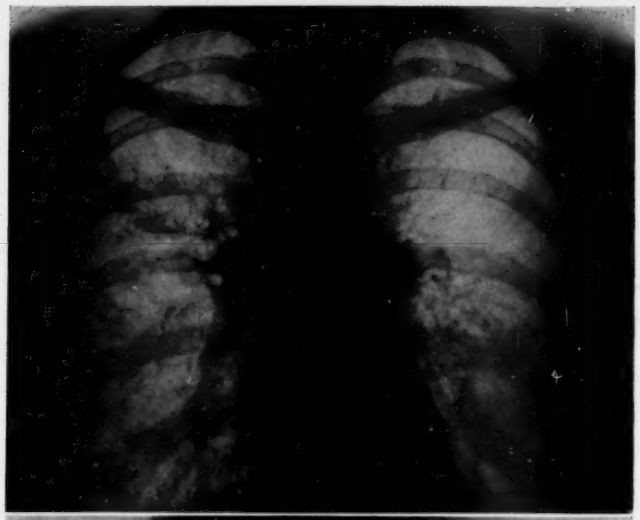

FIG. 2

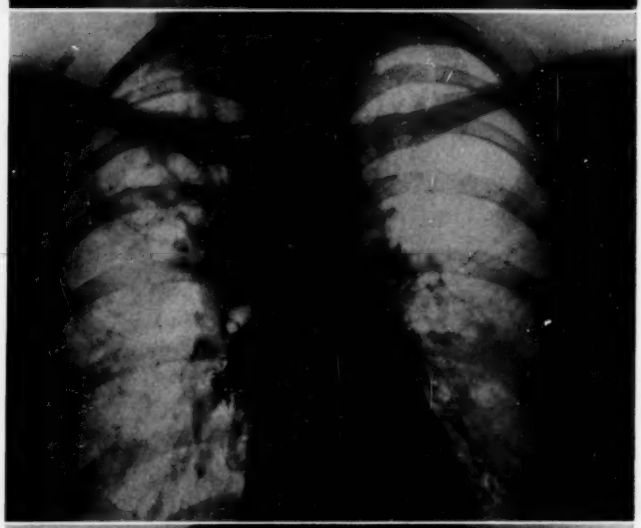

FIG. 3

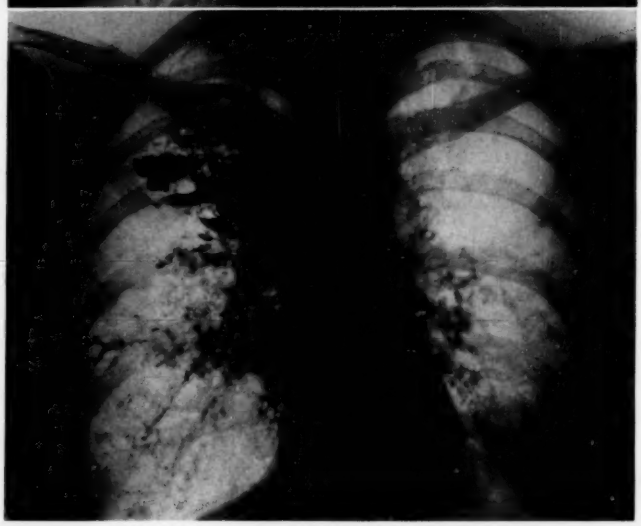

FIG. 1. Chest film on admission

FIG. 2. Film after exacerbation of catarrhal symptoms, showing multilocular cavity-formation.

FIG. 3. Injection of lipiodol into right upper lobe, showing extensive bronchiectatic cavity-formation.

thirds of both lungs. At her first chest examination the breathing was exaggerated on the right to the 2nd rib and 5th vertebral spine, and there were moderately coarse râles on the right to the 2nd rib, and on the left to the 2nd rib and 3rd vertebral spine.

While the lesion in her chest was in the typical location for tuberculosis (figure 1), there were certain features of the X-ray shadows that suggested the possibility of a nontuberculous process, and investigation was therefore turned into that channel. She reacted to 0.000,1 cc. of Old Tuberculin. Lipiodol

FIG. 4. Injection of lipiodol into left upper lobe showing bronchiectasis of some of the bronchi.

injection to the right base showed nothing abnormal. On January 24th, following an acute exacerbation of her catarrhal symptoms with temperature to 99.3°, an X-ray showed on the right side an increase of infiltration in the upper third, bringing into view what appeared to be mutilocular cavity-formation, strongly suggesting bronchiectasis (figure 2). On February 8th, lipiodol was injected into the right upper lobe and the cavity-formation was well outlined (figure 3). Injection of the left upper lobe was not so successful in securing a complete outline of the pathological bronchi, but a number of the trunks were well injected and showed evidence of bronchiectasis (figure 4).

Apparently better drainage of the cavities on the right was established following the injection of lipiodol, for the breath-sounds became amphoric, there was a cracked-pot sound, and bronchophony and posttussive suction were heard over that area. Moderately coarse râles were heard also at the left apex at all examinations.

She had bloody sputum on six occasions. The sputum was negative.

A diagnosis of nontuberculous bronchiectasis was made and she was returned to her former physician for further treatment. She spent the following month in Florida, leading an active social life and spending much time on the beach. She was well tanned, and her cough and expectoration improved, but she lost 13 lbs. in weight. She felt generally well. Several months later she died, apparently of pneumonia, but full details could not be obtained.

## COMMENT

This case is reported because of the unusual localization of a nontuberculous bronchiectasis in the upper part of both lungs. It is a striking exception to the general rule that chronic bilateral lesions in the upper third of the lungs usually are tuberculous.

It has been suggested that this patient represents a case of cystic disease of the lung. While this may be possible, we feel that the authenticity of the diagnosis would justly be challenged if it were so presented. In favor of such a diagnosis is the cellular appearance of the second right interspace on the chest-film at admission; this appearance is accentuated on the film after exacerbation of the catarrhal symptoms, and a larger cavity is vaguely outlined at the apex. The shapely rounded character of the annular shadows, although not perfectly circular, is very suggestive of cystic disease. The long history of cough and expectoration is compatible with either cystic disease of the lung or bronchiectasis. Cysts are said to be very easy to fill with lipiodol, and bronchiectatic cavities difficult; if this is true the beautiful filling of the right upper lobe speaks in favor of cystic disease, and the poor filling of the left in favor of bronchiectasis. The instability of the shadows argues strongly against cystic disease, except under conditions that we shall discuss later.

Although Wood in a careful analysis of the clinical syndrome considered dyspnoea the most constant subjective complaint in cystic disease, and this patient complained of a slight degree of dyspnoea, it seems not unlikely that any pulmonary lesion as extensive as hers might produce slight dyspnoea. Considerable amounts of sputum, cyanosis and pulmonary haemorrhage were all rare in his series.

Rather than the diminution of breath-sounds, vocal resonance and vocal fremitus found in cases of cystic lung, this patient had an exaggeration of breath-sounds at the right top over the lesion. However, these changes in physical signs were probably more characteristic of the large-cell type of cystic disease, as are the contralateral displacement of the trachea and mediastinum and contralateral emphysema.

In the films taken following the injection of lipiodol there is obvious and self-evident bronchiectasis; therefore if this is a case of cystic disease of the lung it is complicated by infection and bronchial dilatation. There is ample other evidence of infection, such as the catarrhal and febrile episodes and the abundance of sputum. This does not, however, rule out the concomitant presence of cystic disease. In fact Sergent calls attention to the frequent association of the small-cell or honeycombed type of cystic disease with infection and bronchiectasis, either congenital or acquired.

It is our belief at the present time that there are certain cases, of which this is an excellent example, in which it is impossible to make a clinical differentiation between bronchiectasis and the small-cell type (the larger retort-shaped cavity and mulberry-shaped cavity in this case do not aid the differentiation either) of cystic disease of the lung with infection and bronchiectasis. We prefer to classify this case as bronchiectasis at present, first of all because there is obviously bronchiectasis present. The history of onset following whooping-cough in childhood, the frequent catarrhal and haemorrhagic episodes, the physical signs and the films following injection of lipiodol are all compatible with bronchiectasis which we know to be a very common disease.

# THE LEUCOCYTIC BLOOD PICTURE IN ACTIVE AND INACTIVE TUBERCULOSIS

## A Comparison of Differential Blood Counts Made during Clinical Activity with Others Made after Clinical Arrest

W. H. MORRISS[1] AND GEORGE C. WILSON[1]

Clinicians, specializing in tuberculosis, have constantly in mind the desire for a better index to measure the improvement or advance of disease taking place in their patients. Clinical observation, including vital signs and physical examination, offers much information of value, but fails lamentably in always presenting a true picture of the patient's condition. Frequent serial roentgenograms have added much to an understanding of our patients' true status, but there is frequently a latent period of a few weeks before new lesions can be detected in the roentgenogram, and from the film alone the determination of satisfactory healing is an uncertain matter even to the expert. It is usually not very difficult, by symptoms, signs and X-ray, to evaluate properly the state of the definitely active or progressive case. The weak point in our therapeutic diagnosis lies in the determination of the time when change of treatment is indicated, when the patient can safely be allowed to return to work, or when artificial pneumothorax can be terminated.

Various laboratory tests have been recommended as aids to fill in this therapeutic gap. Of these, the study of the leucocyte count seems to have much to commend it. Thus Medlar and Pesquera (1) state that "the leucocytes reflect more accurately than do the other clinical findings the actual pathological status of the tuberculous process." Griesbach (2), as quoted in translation by Medlar, puts it even more emphatically: "The differential white blood picture in the hands of an expert is not only indispensable, but the most important adjunct of clinical examination methods in pulmonary tuberculosis . . . and the serial prosecution of hemogram curves . . . permits us to establish prognosis better than any other method of investigation."

Several authors have emphasized the importance of the monocyte-lymphocyte ratio in the differential blood count in tuberculosis (3) (4).

[1] Gaylord Farm Sanatorium, Wallingford, Connecticut.

Medlar, in a most valuable series of papers (5), has taught that the entire blood picture must be considered. He has divided differential counts in tuberculosis into three groups: *first*, the septic type, characterized by a total white count usually above normal, a polymorphonuclear neutrophilic percentage above 65 or 70, a lymphocyte percentage below 25, and a monocyte percentage usually above 8. This type of blood picture, he believes, indicates an active progressive type of disease with probably abscess-formation. The *second* group represents the hyperplastic type, characterized by a total count usually within normal limits, a neutrophilic count below 60 per cent, a lymphocytic count of 25 or more, and a monocytic count above 10 per cent. This picture indicates the formation of new tubercles,—a progressive lesion but one not undergoing abscess-formation. If the lymphocytic percentage is over 30, there is a tendency to heal. The third group constitutes the nonseptic or resistant type, as characterized by a total count never above 10,000, a percentage of lymphocytes that closely approaches that of the neutrophiles, and a monocytic percentage of less than 10. This type-count indicates a healing lesion with well-developed resistance to the disease. Medlar states that the differential count has no value in diagnosis, as there is nothing specific in the reaction, but that, if the diagnosis of tuberculosis is made, the study of blood types does give a most reliable and accurate picture of the pathological changes that are taking place. Several recent papers have corroborated Medlar's findings and endorsed his point of view (6) (7) (8) (9).

At Gaylord Farm Sanatorium there has been great interest in the study of the leucocytic picture in tuberculosis for the last ten years. For most of this time differential counts have been made on admission as a routine, followed by frequent subsequent counts on many of the patients. It has occurred to the authors that a comparative study of counts made while the patients were undergoing treatment in the sanatorium with counts made on the same patients after discharge would be instructive. In the last two years such a study has been made on the patients returning to the ex-patient clinic and is presented in the following paper.

All the patients studied have been under frequent observation, and their convalescence has been followed for a long enough time to form a very accurate picture of their true clinical condition.

*Methods:* The counts made in the sanatorium were done by various laboratory workers, but the work has been under the constant supervision of one of the authors and is believed to be sufficiently constant in technique to offer reliable data. All of the counts made in the clinic were

done by the other author. The differential counts were made on coverslip preparations stained with Wright's stain, with from 200 to 400 cells counted for each differential. Cells were classified into polymorphonuclear neutrophiles, eosinophiles, and basophiles; into lymphocytes, including large, medium and small cells of this type; and into monocytes. In the clinic series the neutrophiles were subdivided into segmented and nonsegmented cells, and the percentage reading of nonsegmented cells was stated in a percentage of the total leucocyte count. The study is based on 201 cases, and includes a study of 579 differential counts. These counts have been classified for tabulation into four groups, using Medlar's septic, hyperplastic, and nonseptic groups as the first three, and adding for the sake of convenience a fourth or normal group, since many counts could not be fitted into any one of Medlar's three groups.

TABLE 1

*Leucocyte grouping in sanatorium patients*

| GROUPS | ACTIVE AND FEBRILE | | ACTIVE AND AFEBRILE | | IMPROVING | | ARRESTED | |
|---|---|---|---|---|---|---|---|---|
| | Number of Counts | Per cent | Number of Counts | Per cent | Number of Counts | Per cent | Number of Counts | Per cent |
| Septic | 24 | 55.8 | 47 | 40.1 | 15 | 18 | 1 | 33.3 |
| Hyperplastic | 13 | 30.2 | 28 | 23.9 | 18 | 21.6 | 0 | 0 |
| Resistant | 0 | 0 | 1 | 0.8 | 6 | 7.2 | 0 | 0 |
| Normal | 6 | 13.8 | 41 | 35 | 44 | 53 | 2 | 66.6 |
| Totals | 43 | 100 | 117 | 100 | 83 | 100 | 3 | 100 |

This normal type is based on the generally accepted standard for a normal differential count. It is characterized by a total count of between 6,000 and 9,000, a neutrophilic percentage between 60 and 70, a lymphocytic percentage between 20 and 30, and a monocytic percentage between 3 and 9. There are, of course, many border-line counts that are difficult to classify. In these cases the decision as to grouping was reached after the total number of each type of cell was calculated, using Medlar's criteria for total counts.

In table 1 the number of counts falling in each blood-group is listed under four clinical heads as follows:

*1:* Cases active and febrile, comprising all patients who at the time of the count were definitely active on the basis of a temperature over 99.6° or pulse over 96, plus an X-ray that was classified as definitely active.

*2:* Cases that at the time of the count were afebrile with no marked elevation of pulse but that had an X-ray film considered as definitely active. These counts were all taken at the time of admission when the patient was starting treatment.
*3:* Cases that were afebrile and improving from the standpoint of clinical observation and X-ray.
*4:* Cases that are considered arrested on the same basis.
The percentages of the clinical group that these numbers constituted are also stated in the table.

In the group of definitely active and febrile cases, which comprises for the most part counts made on admission but also includes counts made while the patients were suffering relapses while under treatment, it will be seen that 86 per cent of the counts show an unfavorable blood picture but 13.8 per cent have a blood picture that shows no noteworthy difference from the normal. In patients considered active but afebrile, 64 per cent have a poor blood picture and 35 per cent are relatively normal. In patients improving satisfactorily under treatment, 39.6 per cent still show unfavorable counts, 53 per cent are normal, and 7.2 per cent show a definitely resistant blood picture. The arrested group is too small to be given consideration. It is to be noted that on many individuals several counts were made, but the patients' clinical status at the time of the count governed the classification into clinical headings.

In table 2 the counts are divided into the same four groups but the clinical condition of the patient is rated on a somewhat different basis into four classes as follows:

*1:* Working full-time
*2:* Working part-time
*3:* Curing and improving
*4:* Curing and doing badly with the disease progressive

It may be noted that in table 2 the patients who are working still show an appreciable percentage of septic counts, —19 per cent in those working full-time and 25.2 per cent in those working part-time. In those patients still under home treatment a fairly high percentage of septic counts is apparent. This latter fact is not surprising, as many of these patients were discharged in unsatisfactory condition and, while showing improvement, are still patients with a doubtful prognosis.

Table 3 is presented to show the change in blood picture that occurred in a group of patients whose clinical condition had changed from that of

active tuberculosis to that of quiescence or arrest of the disease sufficient to permit the patient to engage in part- or full-time work. The comparison is made from two counts on each individual: the one made while the patient is definitely active on the basis of symptoms and X-ray, the second made after he was discharged from the sanatorium for at least a year and is on a working basis. All patients were excluded from this

TABLE 2

*Leucocyte grouping in ex-patients*

| GROUPS | WORKING FULL-TIME | | WORKING PART-TIME | | CURING AND IMPROVING | | CURING WITHOUT IMPROVEMENT | |
|---|---|---|---|---|---|---|---|---|
| | Number of Counts | Per cent | Number of Counts | Per cent | Number of Counts | Per cent | Number of Counts | Per cent |
| Septic | 20 | 19.0 | 24 | 25.2 | 38 | 33.3 | 12 | 63.1 |
| Hyperplastic | 1 | 0.9 | 4 | 4.2 | 11 | 9.6 | 1 | 5.2 |
| Resistant | 10 | 9.5 | 13 | 13.6 | 11 | 9.6 | 1 | 5.2 |
| Normal | 74 | 70.4 | 54 | 56.8 | 54 | 47.3 | 5 | 26.3 |
| Totals | 105 | 99.8 | 95 | 99.8 | 114 | 99.8 | 19 | 99.8 |

TABLE 3

*Changes in blood picture from a count during clinical activity to a count made when the patient had returned to work*

| ACTIVE CASES | WORKING PATIENTS | | | | TOTALS OF ACTIVE CASES |
|---|---|---|---|---|---|
| Blood-groups | *1* Septic | *2* Hyperplastic | *3* Resistant | *4* Normal | |
| *1:* Septic | 13 | 0 | 1 | 18 | 32 |
| *2:* Hyperplastic | 0 | 1 | 4 | 10 | 15 |
| *3:* Resistant | 0 | 0 | 0 | 0 | 0 |
| *4:* Normal | 3 | 0 | 3 | 8 | 14 |
| Totals of working cases | 16 | 1 | 8 | 36 | 61 / 61 |

comparison who came to the ex-patient clinic with a history of recent acute respiratory illness or who had shown any evidence of a relapse.

It must be remembered in reading this table that the clinical change is always a very favorable one, that the time-interval is usually considerably more than one year and that in many cases several years have elapsed between the two counts.

In summary of table 3, groups 1 and 2, the septic and hyperplastic

groups, may be considered as definitely unfavorable, and groups 3 and 4 as favorable.

Of 47 unfavorable blood counts, 32, or 70 per cent, became favorable
Of 14 favorable blood counts, 3, or 21 per cent, became unfavorable
Of 61 active cases, 47, or 77 per cent, had an unfavorable blood picture
Of 61 working cases 44, or 72.1 per cent, had a favorable blood picture

While recognizing the great value of the contribution of Medlar on the importance of considering all types of leucocytes in evaluating the blood picture in tuberculosis, it is felt that the relation between the monocyte and lymphocyte is the most informative part of the picture, an opinion expressed by one of the authors in a former publication (10). In table 4 is presented a comparison between the same group of patients as tabu-

TABLE 4

*Changes in blood picture, as shown in L/M Index from a count during clinical activity to a count made when returned to work*

| ACTIVE CASES | WORKING PATIENTS | | | | TOTALS OF ACTIVE CASES |
|---|---|---|---|---|---|
| L/M Index | 0–1 | 1.1–2 | 2.1–3 | 3.1 + | |
| L/M: 0–1 | 0 | 0 | 1 | 7 | 8 |
| L/M: 1.1–2 | 0 | 1 | 3 | 17 | 21 |
| L/M: 2.1–3 | 0 | 0 | 0 | 14 | 14 |
| L/M: 3.1+ | 0 | 1 | 4 | 12 | 17 |
| Totals of working cases | 0 | 2 | 8 | 50 | 60 / 60 |

lated in table 3, in which the ratio between lymphocytes and monocytes is divided into four groups, as follows:

*1:* A ratio of between zero and one
*2:* A ratio of from 1.1 to 2
*3:* A ratio of between 2.1 and 3
*4:* A ratio of more than 3.1

Groups 1 and 2 may be considered as definitely active, group 3 as probably active, and group 4 as a normal ratio.

A summary of table 4 shows a slightly higher agreement with expectation, thus:

Of 43 counts with an unfavorable L/M index, 38, or 88.3 per cent, became favorable

Of 17 counts with a favorable L/M index, 5, or 29.4 per cent, became unfavorable
Of 60 active cases, 43, or 71.6 per cent, had an unfavorable L/M index
Of 60 working cases, 50, or 83.3 per cent, had a favorable L/M index

The study of the proportion of nonsegmented neutrophiles added little information of value, for such counts were made only on the clinic cases, so that no comparison could be made. Of the 270 counts in which this differentiation was made, in 26 the percentage of nonsegmented cells was above five, a percentage of the entire leucocyte count that may be taken as the upper limit of normal. Of these 26 counts, 14 occurred in counts classified as septic, 2 in hyperplastic counts, 1 in resistant, and 8 in the normal group. Of the 9 unfavorable percentages that occurred in otherwise favorable counts, in 2 instances the findings may have been suggestive of otherwise unsuspected activity. There were many counts classified as septic that had a normal proportion of nonsegmented cells: thus, in the 112 counts with a percentage of nonsegmented cells below three, 38 occurred in the septic group. It may well be true that this simplified method of studying the Arneth shift to the left will prove of considerable value in refining and possibly correcting our methods of study of the reactions of the leucocytic picture to disease. Doan (11) has suggested that the same qualitative method of differentiation into mature and immature lymphocytes affords other and useful prognostic indications in the blood picture of tuberculosis.

## DISCUSSION

In the preceding study certain data are presented that may help in estimating the value of the leucocytic blood picture in tuberculosis. It is recognized that the matter is a difficult one, and that the only real estimate as to the value of this examination will have to come through the gradual formation of an opinion as to its usefulness by those employing the procedure in their clinical work. We have attempted to make a comparison that is perhaps too simplified by contrasting the blood picture during clinical activity with that of the same patient after discharge. Only two counts have been considered in the table of actual comparison, and this limitation of counts introduces the element of sampling. It has been pointed out by several authors that any single count is of little value as a prognostic index, but that the series of counts as shown graphically in a haemogram is of great value. While haemograms can be made on

a small series of cases, and perhaps this is the most valuable sort of study in any appraisal of the method, it is usually impossible for any sanatorium to maintain haemograms on all of their patients, and if this is necessary the fact constitutes an important limitation in usefulness of the method. Another criticism may well be raised of this study that has to do with the interpretation of the counts and the technique employed in making them. It is not claimed that in this study any exceptional ability to interpret counts was at hand or that the technique was always in the hands of "superexperts." It is felt, however, that the work is a fair average of interpretation and technique as it must be done in the majority of our tuberculosis sanatoria, and that the method, if it is to be of any considerable use, must not require any exceptional skill.

The tables in this study show an agreement of approximately 75 per cent between blood pictures and clinical condition. On this basis, certainly no sweeping condemnation of the value of leucocyte counting can be made, for few laboratory tests other than specific tests such as the Wassermann can give a better agreement. It is fair however, to point out that as an index of clinical condition, the method from this study has an error of something like 25 per cent. In a large group of patients a study of the blood picture will give a fairly accurate placing of patients in their proper clinical status, but whether Tom Jones can be returned to work on the basis of a good blood picture cannot be safely decided. For instance, we can cite from our records 6 patients who showed in their serial X-rays a definite progression or the development of new infiltration, yet who had a blood picture well within normal limits. When, however, used with correct understanding of its limitations, the procedure has so much worth in improving our understanding of the patients' status that it should be included in our methods of clinical study.

## CONCLUSIONS

1. A study in blood counts in tuberculosis is presented, based on a comparison between the counts made while the patients were clinically active and counts made after discharge from the sanatorium.

2. In the counts made while the patient was clinically active, 86 per cent of the counts were unfavorable, but 13.8 per cent showed a relatively normal picture.

3. In 200 patients who were able to work one year after discharge, 49, or 24.5 per cent, had an unfavorable blood picture and 151, or 75.5 per cent, had a favorable blood picture.

4. A direct comparison of the counts made while the patient was active with a count made when the patient was able to work, showed in the 47 unfavorable counts a favorable change in 32, or 70.2 per cent. In this comparison on 61 cases, 77 per cent had unfavorable pictures while under sanatorium treatment, and 72.1 per cent favorable pictures when they were able to work.

5. When the comparison was based entirely on the change in the L/M Index, the agreement with expectation was a little higher. Thus, of the 43 cases with an unfavorable L/M Index while active, 38, or 88.3 per cent, became normal.

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# INFRAGLOTTIC PERFORATING TUBERCULOUS ULCER OF THE LARYNX[1,2]

FRANK I. PUTNAM

According to a review of literature made by M. Dawson Tyson, and reported in *The Archives of Otolaryngology*, September, 1930, there have only been 8 cases of perforation of the larynx by a tuberculous process reported from 1836 to 1927. The 8 previous cases were as follows: 1848, by Carter; 1879, Gaucher; 1883, Dignot; 1885, Rey; 1894, Vergnioud; 1899, Raviart and Marlier; 1899, Schmit; and 1927, Tyson.

Six cases reported in the same period, in which perforation of the larynx took place by a process that was probably tuberculous, but in which the evidence was not sufficiently conclusive to warrant a definite diagnosis, are also on record as follows: 1836, by Donne; 1851, Fletcher; 1855, Thompson; 1858, Fonrageives; 1860, Rees; and 1891, McLaren.

I wish to here report a case of infraglottic perforating tuberculous ulcer which occurred in March, 1935.

The patient, a white male, aged 59, physician, entered the hospital January 11, 1935, very weak and exhausted from driving part-way from an eastern State in an automobile; however, he was able to sit up in bed and converse freely without fatigue or pain, but with a husky voice. He was able to eat solid food, three meals a day. He stated that he had been compelled recently to give up his practice on account of sickness and exhaustion. He gave a history of having had dyspnoea, increased cough and expectoration during the last four months with irritation and distress in his throat, a feeling of extreme fatigue, and had been losing weight steadily. He had been compelled to give up all work since December, 1934. He had had no previous hospitalization and came to Arizona for climatic reasons. He gave a history of ordinary diseases of childhood and typhoid fever in 1898. He had been refused for military service in 1918 on account of pulmonary tuberculosis. According to his family history, obtained from the patient, there had been no evidence of tuberculosis or cancer in his immediate family. He had had a colonic resection, May, 1927,

[1] Veterans Administration Facility, Tucson, Arizona.

[2] Published with the permission of the Medical Director of the Veterans Administration, who assumes no responsibility for the opinions expressed or the conclusions drawn by the writer.

on account of tuberculosis of the caecum. Following convalescence from this operation, was able to work part-time until December, 1934. On examination he was found to be a poorly nourished man, with sallow color, dry skin, showing moderately cyanotic lips. He appeared very ill and sick. Examination of the larynx showed that the epiglottis was anaemic and arytenoids infantile and oedematous with pear-shaped swelling. The physical examination together with X-ray examination of the lungs were interpreted as far-advanced active tuberculous lesions of both lungs; however, the X-ray of the lungs was interesting and was read as follows:

*Stereo of chest, January 11, 1935:* Contour regular. Trachea midline. Apices and 1st interspaces show light clouding and slight, coarse, irregular, discrete mottling. *Right Lung:* Shows considerable clouding with an intricate network of peribronchial thickening, and some interbronchial clouding from upper border of 4th rib downward, most marked in 4th interspace. *Left Lung:* There is profuse, fine, discrete mottling from lower border of 3rd costal cartilage to base, most marked in 3rd and 4th interspaces. No bronchial dilatations are made out. This basal pathology on both sides is rather sharply limited above, there being a definite separation between the fibrosis at apices and pathology of lower half of lungs. Aortic, cardiac and diaphragmatic shadows normal. *Conclusions:* Pathology at apices and in 1st interspaces is frankly tuberculous in type and shows little if any evidence of present activity. Diffuse pathology lower half of both lungs is decidedly atypical of tuberculosis and is strongly suggestive of diffuse, malignant process.

The physical examination, X-ray and electrocardiograph study of the heart showed moderate impairment of cardiac function, and it was difficult to decide whether this impairment was secondary to pulmonary tuberculosis or whether it was purely a defective heart secondary to general arteriosclerosis and coronary sclerosis. Stereoroentgenograms of chest, January 22, 1935 and March 1, 1935, show very little or no change of the lesions as reported on admission to the hospital. He had from 80 to 90 cc. of a geeenish purulent sputum daily. Sputum was consistently positive for tubercle bacilli. The blood-Wassermann was negative. His temperature ranged from 96° in the early morning up to as high as 104° in the evening until the date of his death.

On February 9, 1935, a small soft nodule formed subcutaneously at left of larynx at border of thyroid cartilage, and apparently fixed to deep tissue of larynx. On February 11, 1935, this became a large fluctuating mass anterior to thyroid cartilage. Under local anaesthetic a transverse incision was made through the skin, superficial fascia and platysma, and 90 cc. of pus drained and a wick inserted. This was dressed, leaving the wound open. Microscopic examination revealed the pus laden with tubercle bacilli; no other organisms were noted. This drained freely for one week and gradually subsided in amount up to date of death, at which time it was still draining.

Contrary to our hopes, the temperature did not subside after draining the cold abscess anterior to the larynx. Dysphagia became present, the epiglottis became enlarged (turban-shaped), while the cords remained normal in color

and the arytenoids had some oedema with pear-shaped swelling. The patient gradually retrogressed until March 20, 1935, on which date he died of general miliary tuberculosis.

*Autopsy examination* of the lungs showed both lungs adherent to chest-wall; thickened pleura, old fibrotic tuberculous lesion of right upper lobe, and both right and left lungs studded with miliary tubercles. In the larynx one large ulcer was noted on the surface of the infraglottic compartment. This extended from the true vocal cords down to the first tracheal ring, and two-thirds of the way around the larynx on the posterior and lateral walls. The mucosa was completely destroyed and the cartilages necrosed. On the left side and near the posterior wall a perforation was found. On microscopic examination miliary tubercles could be seen, and also newly formed connective tissue and lymphocytes. The heart showed coronary sclerosis, and the intestines very extensive tuberculous ulcers throughout both large and small intestines, varying in size from a pin-point to 1.5 inches in diameter, the largest ulcer being at the site of the old operation. Both spleen and kidneys showed miliary tuberculization. The *diagnoses* established were as follows: tuberculosis, pulmonary, miliary, both lungs; tuberculous laryngitis with perforation; arteriosclerosis, coronary; tuberculous enteritis; generalized miliary tuberculosis of kidney and spleen.

## SUMMARY

According to previous reports and a review of the literature, 8 cases of perforation of the larynx by a tuberculous process are reported from 1836 to 1927. Six cases are reported in the same period in which perforation of the larynx took place by a process which was probably tuberculous but in which the evidence was not sufficient to warrant a diagnosis of the disease. The above-reported case makes a series of 9 cases from 1836 to 1935, a period of ninety-nine years.

# A STATISTICAL STUDY OF THE RESULTS OF GROUP TUBERCULIN-TESTING WITH MA-100

**Final Report of The National Tuberculosis Association**

JESSAMINE S. WHITNEY AND ISABEL McCAFFREY

In the course of the investigations sponsored by the Committee on Medical Research of the National Tuberculosis Association, a number of protein substances with high tuberculin activity have been isolated and purified. From the outset it was hoped that practical advantage could be taken of their discovery, for the Committee has consistently taken the stand that the use of a purified product in known concentration was preferable to the use of tuberculin in unknown concentration and mixed with inert substances, as is necessarily the case with the preparations of tuberculin widely used in the past.

Among the first protein substances isolated and purified was one prepared by Masucci and McAlpine (1) and designated MA-100 in conformity with a series of chemical fractions from the tubercle bacillus. This substance was proved by Funk and Huntoon (2) to have high skin-test potency, and its reliability, in comparison with excellent preparations of Old Tuberculin of known value, was confirmed by Mariette and Fenger and their associates (3) in an extended clinical trial.

In view of its apparent reliability, and as a step toward a much desired standardization of procedure and material in the tuberculin testing campaign, the Committee on Medical Research recommended MA-100 to the National Association for trial. As its use continued, however, certain objections developed that have since led to modification of the plan and substitution of another substance, not subject to the same objections. The work of several investigators, especially Aronson and Nicholas (4) had shown that MA-100, while accurate in the detection of hypersensitiveness, might possibly itself sensitize children, leading to false positive reactions. This was not entirely confirmed by other authors, but in the meantime it became evident that a large body of clinicians and epidemiologists in this country were reluctant to break with the traditional use of Old Tuberculin, and would welcome the use of a purified product corresponding to it.

It was a simple step to furnish such a product, as Florence Seibert, working under a grant from the Committee on Medical Research of the National Association, had already laid the groundwork for its production. Continued research resulted in the development of a substance designated Purified Protein Derivative (P.P.D.) which is nonsensitizing, is prepared from a purified type of Old Tuberculin, and is, as far as it is now possible to tell, the active principle of Old Tuberculin itself. A procedure has been worked out permitting its dispensation in exact concentration, comparable to the customary doses of Old Tuberculin, and the results obtained with it may be considered in perfect alignment with the results obtained with the best and most reliable preparations of Old Tuberculin in the past. The details have been recently published by Seibert, Aronson, Reichel, Clark and Long (5).

Nevertheless, in spite of its supersedence by another compound, no one has questioned the reliability of figures obtained with MA-100 as an index of the incidence of tuberculous infection in groups studied for the first time. Hence the following figures have all the value inherent in the results from any potent and reliable tuberculin, and are published accordingly. They furnish a representative picture of the incidence of infection in different age-groups in various parts of the country, and serve to complete the first extensive study with a purified compound.

Early in 1932, the National Tuberculosis Association was authorized by the Medical Research Committee and the Sub-Committee on Clinical Research to offer MA-100 for sale at a reduced price for group-testing in an effort to obtain infection data sufficiently comprehensive to eliminate the individual differences of single groups. This had now been made possible because MA-100 was a standardized tuberculin. This report presents the results of a statistical study of these group tests.

With the vials of MA-100 the National Tuberculosis Association supplied instructions as to dosage and technique and forms for individual and group reporting. The sale of MA-100 was continued for a period of two years, ending in June, 1934. During that time 522 vials of MA-100, and 35,751 individual report-cards were distributed. Of the individual reports, 14,379 were returned to the National Tuberculosis Association and have been tabulated by its Statistical Service.

Of the reports on tests made in this country, 11,836 were sufficiently complete to be included in this study. These reports came from 101 groups in 18 states, as shown in table 1. The smallest group reported

only 3 tests; the largest, 2,258; the average number of tests per group was 117.

The Medical Research Committee recommended that 0.05 cc. of the tuberculin containing 0.0005 mgm. protein be injected for the initial test, with two readings, 24 and 48 hours, respectively, after the injection. However, dosage as reported was not constant for all groups. For 9,638 individual tests in 62 groups included in the study, doses of 0.0005 mgm.

TABLE 1

*Number of groups and tests according to states included in a study of group tuberculin-testing with MA-100 in the United States, 1932–1934*

| STATE | NUMBER OF GROUPS | NUMBER OF TESTS |
|---|---|---|
| *Total* | *101* | *11,836* |
| Arkansas | 2 | 286 |
| California | 6 | 662 |
| Delaware | 7 | 500 |
| Florida | 3 | 230 |
| Georgia | 3 | 85 |
| Illinois | 2 | 43 |
| Indiana | 5 | 155 |
| Kansas | 28 | 893 |
| Minnesota | 1 | 9 |
| Missouri | 5 | 308 |
| Nebraska | 21 | 7,349 |
| New Jersey | 2 | 127 |
| New York | 4 | 234 |
| Ohio | 7 | 393 |
| South Carolina | 2 | 339 |
| Texas | 1 | 21 |
| Utah | 1 | 117 |
| Wisconsin | 1 | 85 |

were reported for the first injection. Sixteen groups with 1,057 tests did not report dosage. In the remaining 1,141 tests, a dose of different size than that recommended was reported, but, in most instances, it has been thought that the error was in reporting rather than in dosage. Therefore all these groups have been included in the statistical study. As to the interval between the injection and the readings, only seven groups including 433 tests reported readings at the two intervals recommended. However, the remainder of the groups reporting this item took the readings sometime between 24 and 48 hours after the injection.

In tabulating the results of MA-100 group-testing, only those definitely

positive were included among the positive reactors, and whenever any doubt was expressed on the record the reaction was classified as negative. It has seemed advisable to eliminate from this study all repeat injections because of the unreliability of a great number of those reported. A second injection, twice the size of the initial dose, was recommended when and only when the first reaction was negative or doubtful. Unfortunately, this procedure was not followed in many of the repeat tests, and hence their elimination.

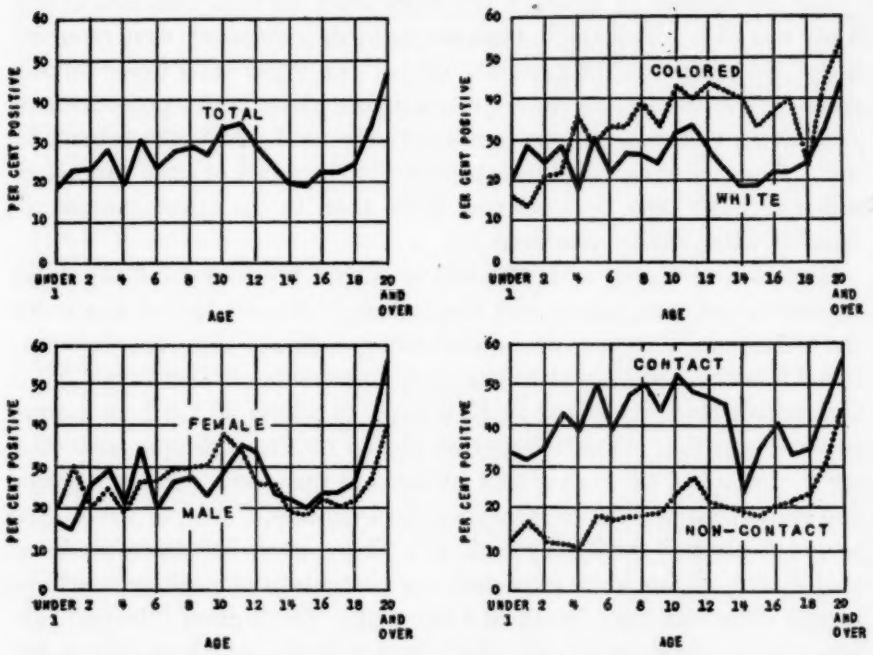
The percentage of positive reactions from all tests included in this study was 25.7. Tuberculin tests among 9,855 individuals were reported either typically rural or typically urban. Of 9,192 tests made among groups of the urban type, that is, coming from places with a population of over 2,500, 22.2 per cent reacted positively to the MA-100 tuberculin test. There were only 663 tests included in the study of rural groups, of which 27.1 per cent, or 5 per cent more than in the urban groups, responded with positive reactions.

Groups were tested with MA-100 in clinics, hospitals, and sanatoria (including patients, nurses, and employees), children's homes, homes for the feeble-minded, preventoria, elementary schools, high-schools, vocational schools, and normal colleges and universities. There were 6,970 high-school students tested in 12 groups, of whom 20.1 per cent were positive reactors. Omaha reported eleven of these groups, with 98.1 per cent of all of the high-school students in the study. Eleven groups in 6 states reported 789 elementary school-children tested, of whom 26.6 per cent showed positive reactions. There were 707 tests made at clinics, and, as would be expected, the percentage of positive reactions among them was high, being 36.9 per cent. The highest infection rate was reported from groups of sanatorium patients, of whom 230 of 309 tested showed evidence of tuberculous infection. Nurses and hospital and santorium employees showed an infection rate considerably higher than the average. The rate was found to be lower than the average among a group of preschool and preventorium children recommended for special nutritional care.

Classifying the 11,836 tests included in the report according to the ages of the persons tested, there were found to be more boys and girls 15 years of age than there were in any other age-group. The highest percentage of positive reactors, excluding those 20 years of age and over, was 34.6 among those 11 years old. The general trend of tuberculous

infection was upward to the early teen ages, when the proportion of postive reactors began to decrease. However, the proportion of positive reactors again began to rise steadily in the late teens. This was true alike for white and colored, males and females, and contact and non-contact cases, as shown in the accompanying charts.

Colored persons tested comprised only 8 per cent of the entire report. The percentage of positive reactors among them was 38.4 per cent as against 24.6 per cent positive white reactors. It will be noted that the




Percentage of positive reactors among the entire group, white and colored, males and females, and contacts and noncontacts included in a study of group tuberculin-testing with MA-100 in the United States, 1932–1934.

infection rate indicated for the colored groups was higher than for the whites, but the difference is not so great as in the tuberculosis mortality rates. The colored infection rate reported was one and one-half times the white infection rate, while during 1931 and 1932 three and one-half times as many colored people as whites in proportion to their numbers died of tuberculosis in the United States Death Registration Area. During the first four years of life the infection rate of white groups reported was higher than that of the colored groups. During the fifth year of life

and at each age afterward, with few exceptions, the proportion of positive reactors to MA-100 was considerably greater among the colored tested than among the whites. Among the colored included in the analysis of MA-100 tuberculin-testing, the percentages of infection in the three age-

TABLE 2

*Results of group tuberculin-testing with MA-100 in the United States by age and color, 1932–1934*

| AGE | TOTAL | | WHITE | | COLORED | |
|---|---|---|---|---|---|---|
| | Number tested | Per cent positive | Number tested | Per cent positive | Number tested | Per cent positive |
| *All ages* | *11,836* | *25.7* | *10,876* | *24.6* | *960* | *38.4* |
| Under 1 | 48 | 18.8 | 36 | 19.4 | 12 | 16.7 |
| 1 | 43 | 23.3 | 28 | 28.6 | 15 | 13.3 |
| 2 | 68 | 23.5 | 49 | 24.5 | 19 | 21.1 |
| 3 | 87 | 27.6 | 73 | 28.8 | 14 | 21.4 |
| 4 | 157 | 19.7 | 140 | 17.9 | 17 | 35.3 |
| 5 | 151 | 30.5 | 123 | 30.9 | 28 | 28.6 |
| 6 | 272 | 23.5 | 233 | 21.9 | 39 | 33.3 |
| 7 | 310 | 27.4 | 252 | 26.2 | 58 | 32.8 |
| 8 | 343 | 28.6 | 282 | 26.2 | 61 | 39.3 |
| 9 | 327 | 26.6 | 255 | 24.7 | 72 | 33.3 |
| 10 | 357 | 33.3 | 304 | 31.6 | 53 | 43.4 |
| 11 | 373 | 34.6 | 326 | 33.7 | 47 | 40.4 |
| 12 | 348 | 29.0 | 309 | 27.2 | 39 | 43.6 |
| 13 | 582 | 24.2 | 537 | 22.7 | 45 | 42.2 |
| 14 | 1,307 | 20.3 | 1,255 | 19.4 | 52 | 40.4 |
| 15 | 1,908 | 19.3 | 1,844 | 18.9 | 64 | 32.8 |
| 16 | 1,741 | 22.6 | 1,662 | 21.9 | 79 | 36.7 |
| 17 | 1,296 | 22.5 | 1,244 | 21.7 | 52 | 40.4 |
| 18 | 622 | 24.0 | 597 | 24.0 | 25 | 24.0 |
| 19 | 313 | 32.9 | 295 | 32.2 | 18 | 44.4 |
| 20 and over | 1,027 | 46.4 | 886 | 45.1 | 141 | 54.6 |
| Age unknown | 156 | 25.6 | 146 | 25.3 | 10 | 30.0 |
| Under 5 | 403 | 22.3 | 326 | 22.4 | 77 | 22.1 |
| 5– 9 | 1,403 | 27.1 | 1,145 | 25.5 | 258 | 34.1 |
| 10–14 | 2,967 | 25.4 | 2,731 | 24.0 | 236 | 41.9 |
| 15–19 | 5,880 | 22.2 | 5,642 | 21.6 | 238 | 35.7 |

groups, 5 to 9, 10 to 14, and 15 to 19, were between one and two times the infection percentages of the whites tested in the same age groups. However, the colored tuberculosis-mortality rates in the United States Death Registration Area are approximately five times the white mortality rates in each of these age-groups. We have not yet arrived at any satisfactory

explanation of these amazing differences between white and colored infection and mortality rates.

The sexes were approximately evenly represented in the tests reported. The males showed a slightly higher percentage of positive reactors than

TABLE 3

*Results of group tuberculin-testing with MA-100 in the United States by age and sex, 1932–1934*

| AGE | TOTAL | | MALE | | FEMALE | |
|---|---|---|---|---|---|---|
| | Number tested | Per cent positive | Number tested | Per cent positive | Number tested | Per cent positive |
| *All ages* | *11,836* | *25.7* | *5,617* | *26.5* | *6,219* | *25.0* |
| Under 1 | 48 | 18.8 | 18 | 16.7 | 30 | 20.0 |
| 1 | 43 | 23.3 | 20 | 15.0 | 23 | 30.4 |
| 2 | 68 | 23.5 | 39 | 25.6 | 29 | 20.7 |
| 3 | 87 | 27.6 | 51 | 29.4 | 36 | 25.0 |
| 4 | 157 | 19.7 | 76 | 21.1 | 81 | 18.5 |
| 5 | 151 | 30.5 | 66 | 34.8 | 85 | 27.1 |
| 6 | 272 | 23.5 | 138 | 20.3 | 134 | 26.9 |
| 7 | 310 | 27.4 | 168 | 26.2 | 142 | 28.9 |
| 8 | 343 | 28.6 | 166 | 27.7 | 177 | 29.4 |
| 9 | 327 | 26.6 | 160 | 23.1 | 167 | 29.9 |
| 10 | 357 | 33.3 | 173 | 28.9 | 184 | 37.5 |
| 11 | 373 | 34.6 | 199 | 35.2 | 174 | 33.9 |
| 12 | 348 | 29.0 | 152 | 32.9 | 196 | 26.0 |
| 13 | 582 | 24.2 | 274 | 23.4 | 308 | 25.0 |
| 14 | 1,307 | 20.3 | 608 | 21.7 | 699 | 19.0 |
| 15 | 1,908 | 19.3 | 902 | 20.6 | 1,006 | 18.2 |
| 16 | 1,741 | 22.6 | 861 | 23.5 | 880 | 21.7 |
| 17 | 1,296 | 22.5 | 701 | 24.1 | 595 | 20.5 |
| 18 | 622 | 24.0 | 316 | 26.3 | 306 | 21.6 |
| 19 | 313 | 32.9 | 131 | 40.5 | 182 | 27.5 |
| 20 and over | 1,027 | 46.4 | 323 | 57.0 | 704 | 41.6 |
| Age unknown | 156 | 25.6 | 75 | 29.3 | 81 | 22.2 |
| Under 5 | 403 | 22.3 | 204 | 23.0 | 199 | 21.6 |
| 5– 9 | 1,403 | 27.1 | 698 | 25.5 | 705 | 28.7 |
| 10–14 | 2,967 | 25.4 | 1,406 | 26.0 | 1,561 | 24.9 |
| 15–19 | 5,880 | 22.2 | 2,911 | 23.8 | 2,969 | 20.6 |

did the females, the rate for males being 26.5 per cent and that for females 25.0 per cent. Boys from 6 to 10 years of age showed less evidence of tuberculous infection than did the girls of the same ages, but at almost every other age there was a greater proportion of male positive reactors to MA-100 than female positive reactors in the same age-groups.

Of the persons known to have a history of contact with tuberculosis, almost twice as many reacted positively as did those with no tuberculosis contact. The disparity between the percentage of positive reactors among these two classifications was greatest in the fourth and fifth years

TABLE 4

*Results of group tuberculin-testing with MA-100 in the United States among contacts and non-contacts by age, 1932–1934*

| AGE | CONTACT | | NON-CONTACT | |
|---|---|---|---|---|
| | Number tested | Per cent positive | Number tested | Per cent positive |
| *All ages* | *2,079* | *41.3* | *9,757* | *22.4* |
| Under 1 | 15 | 33.3 | 33 | 12.1 |
| 1 | 19 | 31.6 | 24 | 16.7 |
| 2 | 35 | 34.3 | 33 | 12.1 |
| 3 | 44 | 43.2 | 43 | 11.6 |
| 4 | 53 | 37.7 | 104 | 10.6 |
| 5 | 59 | 49.2 | 92 | 18.5 |
| 6 | 84 | 39.3 | 188 | 16.5 |
| 7 | 99 | 47.5 | 211 | 18.0 |
| 8 | 112 | 50.0 | 231 | 18.2 |
| 9 | 105 | 43.8 | 222 | 18.5 |
| 10 | 118 | 52.5 | 239 | 23.8 |
| 11 | 122 | 48.4 | 251 | 27.9 |
| 12 | 104 | 47.1 | 244 | 21.3 |
| 13 | 91 | 45.1 | 491 | 20.4 |
| 14 | 278 | 23.7 | 1,029 | 19.3 |
| 15 | 162 | 34.0 | 1,746 | 18.0 |
| 16 | 154 | 40.9 | 1,587 | 20.8 |
| 17 | 107 | 32.7 | 1,189 | 21.5 |
| 18 | 62 | 33.9 | 560 | 22.9 |
| 19 | 37 | 45.9 | 276 | 31.2 |
| 20 and over | 205 | 55.6 | 822 | 44.2 |
| Age unknown | 14 | 28.6 | 142 | 25.4 |
| Under 5 | 166 | 37.3 | 237 | 11.8 |
| 5– 9 | 459 | 46.0 | 944 | 17.9 |
| 10–14 | 713 | 38.8 | 2,254 | 21.2 |
| 15–19 | 522 | 36.6 | 5,358 | 20.8 |

of life and became progressively less in the older age-groups. Tuberculous infection increased with age generally at a more rapid rate among the noncontacts than among the contacts. It seems altogether probable that some of those included in the noncontact class were subjected to more frequent casual contact with tuberculosis as they grew older. This

possibly accounts, in part at least, for the increasing incidence of infection among them.

The National Tuberculosis Association sought to classify the results of MA-100 tuberculin tests according to the nativity and parentage of those tested. Of the 10,876 white persons tested, 10,838 reported both their own and their parents' nativity. There were 71.8 per cent native-born of native parentage, 26.5 per cent native-born of foreign or mixed parentage, and 1.7 per cent foreign-born. The nativity of the parents did not seem to be a significant factor in tuberculous infection among native-born children. The infection rate for those of native parentage was 24.2 per cent, and for those of foreign or mixed parentage, the rate was 24.7 per cent.

As shown in table 5, up to 15 years of age (with the exception of girls less than 5 years old) both males and females native-born of native parentage reacted positively to the MA-100 tuberculin test in greater numbers proportionately than did the native-born of foreign or mixed parentage. However, from fifteen to nineteen years of age there was a slightly higher percentage of positive reactors among those born of foreign or mixed parentage than among those of native stock, while adults 20 years of age and over showed a considerably higher proportion of positive reactors among the group of foreign extraction.

In cases of foreign or mixed parentage, the father's country of birth was tabulated except when the father was native-born, in which case the mother's country of birth was tabulated. There were 2,873 tests made on native-born Americans of foreign parentage, and a classification of the results of the tests according to the country of parentage is shown in table 6. Of the 15 countries listed, in each of which parents of fifty or more of those tested were born, all but one are European countries. The exception is Canada. The highest percentage of positive reactors was found among children of Yugoslavian parentage, with 35.2 per cent of the tests evidencing tuberculous infection. Those of German descent, of whom 276 were tested, came next, with 27.9 per cent positive reactions. The lowest percentage was found among the native-born of Hungarian extraction, among whom 72 tests were made, 13.9 per cent responding with positive reactions.

Unfortunately, the small number of tests reported on persons of foreign birth, only 179, is too small for statistical survey as to sex, age, and nationality. In passing, however, it may be noted that the percentage of positive reactors was nearly twice as high as it was among the native-

born Americans and that a markedly higher infection rate is indicated for the foreign-born from each country than for those removed from the same country by one generation.

TABLE 5

*Results of group tuberculin-testing with MA-100 in the United States according to nativity, parentage, age and sex, 1932–1934*

| NATIVITY AND PARENTAGE BY AGE | TOTAL | | MALE | | FEMALE | |
|---|---|---|---|---|---|---|
| | Number tested | Per cent positive | Number tested | Per cent positive | Number tested | Per cent positive |
| *Native-born of native parentage* | | | | | | |
| *All ages* | *7,786* | *24.2* | *3,664* | *25.4* | *4,122* | *23.1* |
| Under 5 | 259 | 23.6 | 130 | 24.6 | 129 | 22.5 |
| 5– 9 | 971 | 26.3 | 490 | 25.7 | 481 | 26.8 |
| 10–14 | 1,992 | 24.6 | 947 | 25.1 | 1,045 | 24.2 |
| 15–19 | 3,868 | 21.0 | 1,870 | 23.0 | 1,998 | 19.1 |
| 20 and over | 586 | 40.8 | 173 | 50.9 | 413 | 36.6 |
| Age unknown | 110 | 20.9 | 54 | 25.9 | 56 | 16.1 |
| *Native-born of foreign or mixed parentage* | | | | | | |
| *All ages* | *2,873* | *24.7* | *1,434* | *25.5* | *1,439* | *24.0* |
| Under 5 | 61 | 19.7 | 34 | 11.8 | 27 | 29.6 |
| 5– 9 | 159 | 22.6 | 84 | 19.0 | 75 | 26.7 |
| 10–14 | 692 | 22.0 | 334 | 24.6 | 358 | 19.6 |
| 15–19 | 1,700 | 22.6 | 905 | 24.0 | 795 | 21.1 |
| 20 and over | 228 | 49.1 | 63 | 63.5 | 165 | 43.6 |
| Age unknown | 33 | 39.4 | 14 | 42.9 | 19 | 36.8 |
| *Foreign born* | | | | | | |
| *All ages* | *179* | *44.1* | *92* | *47.8* | *87* | *40.2* |
| Under 5 | 2 | — | 2 | — | — | — |
| 5– 9 | 7 | 14.3 | 5 | 20.0 | 2 | — |
| 10–14 | 38 | 23.7 | 14 | 28.6 | 24 | 20.8 |
| 15–19 | 64 | 34.4 | 32 | 31.3 | 32 | 37.5 |
| 20 and over | 67 | 68.7 | 39 | 74.4 | 28 | 60.7 |
| Age unknown | 1 | 100.0 | — | — | 1 | 100.0 |

This report is limited to the results of the 11,836 tests reported in continental United States. Nearly 1,400 tests were reported by groups in Hawaii, the Philippine Islands, Puerto Rico, and Nova Scotia. Because of special conditions, these have not been included in the total

analysis. MA-100 tuberculin tests were applied to a group of 275 high-school students in Honolulu of Hawaiian and Hawaiian-mixed blood and ranging in age from 11 to over 20 years. Positive reactions indicating tuberculous infection resulted from 45.8 per cent of the initial injections, an infection percentage over twice that of the American high-school students included in the study. The Hawaiian boys responded with a greater proportion of positive reactors than did the girls, and this is especially observed among those of Asiatic-Hawaiian and mixed Hawaiian

TABLE 6

*Results of group tuberculin-testing with MA-100 in the United States among native-born of foreign or mixed parentage according to the country of birth of the parents, 1932–1934*

| NATIVITY AND PARENTAGE | TOTAL | | MALE | | FEMALE | |
|---|---|---|---|---|---|---|
| | Number tested | Per cent positive | Number tested | Per cent positive | Number tested | Per cent positive |
| *Native-born of foreign or mixed parentage* | 2,873 | 24.7 | 1,434 | 25.5 | 1,439 | 24.0 |
| *Country of birth of parents* | | | | | | |
| Austria | 75 | 26.7 | 36 | 30.6 | 39 | 23.1 |
| Bohemia | 107 | 25.2 | 55 | 21.8 | 52 | 28.8 |
| Canada | 73 | 24.7 | 37 | 18.9 | 36 | 30.6 |
| Czechoslovakia | 187 | 18.2 | 88 | 21.6 | 99 | 15.2 |
| Denmark | 168 | 19.0 | 75 | 22.7 | 93 | 16.1 |
| England | 125 | 24.8 | 68 | 23.5 | 57 | 26.3 |
| Germany | 276 | 27.9 | 126 | 28.6 | 150 | 27.3 |
| Hungary | 72 | 13.9 | 33 | 15.2 | 39 | 12.8 |
| Ireland | 130 | 21.5 | 60 | 30.0 | 70 | 14.3 |
| Italy | 401 | 26.9 | 234 | 26.1 | 167 | 28.1 |
| Lithuania | 65 | 27.7 | 27 | 25.9 | 38 | 28.9 |
| Poland | 220 | 23.2 | 122 | 23.0 | 98 | 23.5 |
| Russia | 276 | 26.1 | 152 | 30.3 | 124 | 21.0 |
| Sweden | 263 | 20.9 | 98 | 16.3 | 165 | 23.6 |
| Yugoslavia | 54 | 35.2 | 31 | 32.3 | 23 | 39.1 |
| All others | 381 | 28.9 | 192 | 29.2 | 189 | 28.6 |

blood. A group of infants, preschool, elementary and high-school children in Manila, all of whom were contacts, had an infection rate of 70.5 per cent, or one and three-quarters times the rate for all contacts in the report of tests made in the United States. It was also higher than the infection percentage in a Nova Scotia sanatorium where 65.8 per cent of the patients reacted positively. The initial test on a group of children in Puerto Rico who were 16 years of age and under revealed that 51.5 per cent were infected with tuberculosis. This is not surprising when the extremely high tuberculosis mortality rate in Puerto Rico is considered.

It is, of course, recognized that these foreign and insular reports of MA-100 tests are insufficient to form the basis of a statistical study leading to valid conclusions.

## SUMMARY

This study was undertaken by the National Tuberculosis Association as an experiment. It was hoped that we might obtain statistics from which conclusions could be deduced that would be useful for reliable, direct comparisons. Heretofore, it had been difficult to find groups capable of statistical comparison because of variations in dosage and technique. With the standardization of MA-100 as to tuberculin dosage and technique, it became possible for the first time to summarize groups with the result that unusual and individual variations from the norm are minimized. Thus we have approached an average which it is believed may be validly used for comparison. The following significant findings are based upon a total of 11,836 MA-100 tuberculin tests in 101 groups of varying sizes and types classified according to age, sex, color, tuberculous contact, nativity, and parentage:

1. Postive reactions resulted from 25.7 per cent of the 11,836 tests included in the study.

2. The trend of tuberculous infection among males, females, white, colored, contacts, and noncontacts was generally upward to the early teen ages when the proportion of positive reactors began to decrease. However, the percentage of positive reactors to MA-100 was found to increase and rise steadily again in the late teen ages.

3. The 960 colored persons tested showed a tuberculosis infection rate one and one-half times the white rate. Thirty-eight per cent of the colored and 25 per cent of the 10,876 white persons tested showed positive reactions. Tuberculous infection was not so prevalent among the colored as might be expected from a comparison of white and colored mortality rates. Three and one-half times as many colored people as whites died of tuberculosis in proportion to their numbers in the United States Death Registration Area in 1931 and 1932.

4. The sexes were approximately evenly represented in the tests reported and the proportion of positive reactors among them was approximately the same, 26.5 per cent of the tests among males and 25.0 per cent of the tests among females resulting in positive reactions. At almost every age, except from 6 to 10, there was a higher percentage of positive male reactors to MA-100 than female positive reactors at the same age.

5. Almost twice as many persons known to have a history of contact with tuberculosis reacted positively to MA-100 as did those with no history of contact. Forty-one per cent of the 2,079 persons reported to be contacts evidenced tuberculous infection while only 22 per cent of the 9,757 persons classed as noncontacts reacted positively. Tuberculous infection increased with age generally at a more rapid rate among the noncontacts than among the contacts.

6. The nativity of the parents did not seem to be a significant factor in tuberculous infection among native-born children. For those of native parentage, the infection rate was 24.2 per cent, and for those of foreign or mixed parentage the rate was 24.7 per cent.

7. The percentage of positive reactors among native born was only half as high as the infection rate found among the foreign born. However, only 179 of the individuals included in this study were reported as foreign-born. A markedly higher infection rate was indicated for the foreign-born from each country than for those removed from the same country by one generation.

The collection of data is being continued by the National Tuberculosis Association under the direction of the Tuberculin Committee, a Sub-Committee of the Medical Research Committee, the distribution of Purified Protein Derivative (P.P.D.) replacing the distribution of MA-100. When this work is completed, we shall have studied a larger group and therefore will be in a position to present more significant figures.

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# SAPROPHYTIC ACID-FAST BACILLI FROM URETERAL SPECIMENS[1]

ARTHUR H. WELLS

For a period of several months we had been finding rare slender and beaded acid-fast bacilli, morphologically typical of tubercle bacilli, in the majority of cystoscopic specimens from the urinary bladder and kidney pelves. These were never found to be pathogenic for guinea pigs nor did they "culture out" as *M. tuberculosis* on Corper's potato media; nevertheless at times they caused considerable concern. Suddenly, large numbers of these organisms were found in kidney-pelves washings in two consecutive cases, in both of which tuberculosis was entirely unsuspected. An immediate search of all possible sources of contamination disclosed myriads of acid-fast bacilli, mixed with a few fungi, in the rubber tubing of the irrigating apparatus used to wash out the kidney pelves, also in both mercury-cyanide solutions.

The apparatus had been routinely washed out with a mercury-cyanide solution, 1–1000, allowing the cyanide to remain in it approximately twenty minutes. Then it was filled with a mercury-cyanide solution, 1–5000, which solution was used by the urologist in the cystoscopy. Both solutions remaining in the apparatus were returned to their original bottles, so that these were apparently contaminated from the living organisms in the rubber tubing. Smears from distilled water and cyanide tablets (used in the irrigating solutions), also lubricating jelly, room-dust, ureteral catheters and other urological apparatus failed to reveal any acid-fast bacteria. Other similar irrigating apparatus in other parts of the hospital, sterilized by other means and used for other purposes, as well as a great variety of rubber tubing, catheters and metal water-taps throughout the hospital, revealed no acid-fast bacilli.

Following these findings, the glass portion of the contaminated urological irrigating apparatus was carefully cleaned by boiling, new tubing applied and new cyanide solutions prepared in new sterile bottles. The same but possibly more careful routine preoperative preparation of the

[1] From the William Volker Laboratory, Research Hospital, Kansas City, Missouri.

apparatus ensued. One month later, large numbers of the same acid-fast bacteria were found in the tubing after another surprising finding of acid-fast bacilli in kidney washings. A repetition of careful cleaning, application of new tubing and change in technique of sterilizing the apparatus by allowing the 1–5000 cyanide solution to remain in it constantly, resulted in a successful disappearance of the saprophytes for a period of more than two years.

The microörganism was isolated without difficulty by fishing single colonies from agar plates. They maintained their slender, beaded morphology, but almost completely lost the property of retaining carbol-fuchsin when stained by the Ziehl-Neelsen method. The first cultivation on artificial media resulted in only rare organisms staining acid-fast. In subsequent subcultures, it was difficult to find any acid-fast bacteria. Attempts were made to return the staining to its original acid-fast character by subculturing on a great variety of combinations of media, including milk, butter, egg, petrolatum, olive oil, mineral oil, stop-cock jelly, paraffin, prairie hay, alfalfa, rosin, cottonseed oil, tannic acid, glycerine, iron, copper, tin, mercury, mercury cyanide, sulphur, saline and distilled water. If the organism grew at all on any of this bizarre array of media and laboratory products, it would not maintain or return to its acid-fast character, even after prolonged periods of cultivation at varied temperatures. However, subculturing on the cleaned and sterilized original rubber tubing resulted, after three weeks, in the appearance of tiny grayish granules on the cut-edges of the tubing, which growth proved to be 100 per cent acid-fast, slender, beaded bacteria. This also occurred on rubber tubing previously extracted with ether and chloroform, and the acid-fast property of the bacteria was not altered by prolonged extraction with the two fat solvents.

The organism is gram-positive, generally beaded, and averages very slightly larger than tubercle bacilli in both length and breadth. It is nonmotile. It grows abundantly on all ordinary bacterial media in 24 hours and has a rather dull-yellow pigment. On agar the moderately large dull-yellow colonies are round, smooth, soft, shiny, dome-shaped and have smooth edges. In beef-broth and litmus milk, a thick, dirty, yellow scum forms on the surface after 72 hours. The milk is not otherwise altered and there is no acid- or gas-formation in dextrose, lactose, mannite, saccharose, maltose or salcin sugar media. Gelatin is not liquefied, although there is a heavy growth on its surface. Nitrates are not reduced. An unusually luxuriant and slimy yellow growth covers

potato media in 72 hours. Although it grows in the ice-box or in the 37° incubator, room temperature proves optimum.

The organism is unusually resistant to certain destructive agents. It remains viable on rubber tubing over six months, and disappeared after a year. Mercury cyanide, 1–1000, destroys it in 20 minutes, while in a dilution of 1–5000 it survives 72 hours. Phenol, 1–1000, does not destroy it in ten days. It will not grow after 2 minutes in merthyolate, 1–1000, or in a 0.2 per cent solution of gentian-violet.

In the inoculation of guinea pigs, generally no lesions appear after six weeks. Occasionally, however, a dozen or more, gray, 1 mm. in diameter, round discrete lesions were found in the spleen and liver, and once in the lungs. Grossly, these might be mistaken for tubercle nodules. Careful microscopic differentiation is necessary. The lesions have a centre filled with neutrophiles, surrounded by a rather thick and hyalinized wall of fibroblasts. There are rare giant cells. Using Brown-Breen and acid-fast stains, no demonstrable bacteria were found in paraffin sections of these lesions.

## DISCUSSION

The wide distribution of acid-fast saprophytic bacteria in nature is a characteristic of the genus. Neisser (1) concluded that the organisms isolated from water-taps, sand-filters, springs, rubber tubes etc., have a single origin, the great realm of soil acid-fast bacilli. Frey and Hagan (2) found them in all of 100 samples of soil collected from many parts of the United States and other countries. The common occurrence of *Mycobacterium smegmatis* about the genitalia is accepted; however, acid-fast saprophytes are much less frequently found elsewhere on the body. Their ability to exist about distilled-water reservoirs, metal taps, sinks, in dust and in chemicals has been shown by Neisser (1), Eichbaum (3), Wilson (4), and many others, as a dangerous source of error in laboratory diagnosis.

Their isolation from mixed cultures has proved an important hindrance in the study of the group. Several unusual and varied methods have been developed. Frey and Hagan (2) used a modification of the Sohngen method to good advantage. Here soil was cultured on paraffin in a salt solution at 47.5°C. to keep down molds and actinomycetes. Eichbaum (3) found that acid-fast organisms would grow in the clear zone about silver and copper, where other bacteria were inhibited. Mudd and Mudd (5) and later Reed and Rice (6) demonstrated that acid-fast bacteria

would pass from a water suspension into oil, whereas other organisms remained in water. Oxalic and acetic acids in low dilutions were found by Corper and Uyei (7) to be deleterious to most bacteria, leaving the acid-fast organisms unharmed. Many other selective media, devised primarily for the isolation of *Mycobacterium tuberculosis*, have not yet been widely adopted for the isolation of the saprophytic members of the genus.

Methods of differentiation and classifications of the saprophytic mycobacteria are far from satisfactory or complete. The organisms are generally designated according to their source of isolation, notwithstanding the possibility of a common source (soil) of the majority. Bergey (8) describes 8 saprophytic species and Lehmann and Neumann (9) name 6 species. That many other species have been and are yet to be described is generally admitted.

For the present, morphology, pigment-production and certain other gross growth characteristics must of necessity play a major rôle in their identification. Standardization of media is important in determining these criteria, for Frey and Hagan (2), working with 75 strains, found that their pigmentation, acid-fast staining and morphology were profoundly changed on varied media; also, that only a rough division into three groups was possible using gross cultural appearances. The importance of utilizable iron in relation to pigmentation is stressed by Reed and Rice (10). Darzine (11) has attempted a differentiation on the basis of a variation in the resistance to decolorization. Cytomorphosis has been demonstrated by Corper (12). The instability or dissociation problem is discussed by Petroff and Steenken (13).

One may conclude from the work of Merrill (14), Kendal, Walker and Day (15), Long and Major (16), and Weinzirl and Knapton (17) that carbohydrate utilization is of but little value in differentiating the individuals of the group. Synthetic inhibiting media was considered of no value by Thomson (18). With certain organic acids, alcohols and amines, Long (19) has divided a small series into three nutritional groups. According to Schlossberger and Pfannenstiel (20) and Neisser (1), nearly all the organisms grow at unusually high temperatures, thus excluding species identification by this means. The absent or low-grade pathogenicity of these organisms for animals is a common characteristic of the group, (Neisser (1), Wilson (4), Thomson (18) and St. John-Brooks (21)).

Distinguishing differences have been found in certain immunological

attributes for rather large groups, but they are rarely species-specific. Allergic skin tests by Krause and Baldwin (22) revealed a strong group-similarity, while Thomson (18) and Frey and Hagan (2) found surprising specificity for three groups. Agglutination and complement-fixation tests proved unsatisfactory because of strong group reactions, inagglutinability of many species, etc. (Koch (23), Twort, Todd and Perkins (24), Harris and Langford (25), Cooke (26)). The experiments of Furth (27) show that only large groups can be separated by complement-fixation and absorption tests. By the use of a method of absorption of agglutins, Wilson (28) found two general groups. Branch (29) reported the isolation of a carbohydrate substance, which gave a precipitate with antisera from different acid-fast bacteria.

The subject of the acid-fast staining property of the mycobacteria and other organisms has received much attention since its discovery by Koch. There is much in the recent literature on the subject which needs clarification. Wherry (30) found that certain acid-fast bacteria become non-acid-fast upon media not readily adopted to the synthesis of fat. This was not entirely verified by Suzenaga (31), and our organism above is an exception. Eberson and Sweeney (32) found certain environmental conditions, such as cultivation on nonprotein simple media, favored loss of acid-fastness. Maher (33) caused certain common bacteria to become acid-fast by growing them under adverse conditions. Campbell (34), repeating the work of Bienstock and Gottstein, could not verify their findings that certain common bacteria would become acid-fast when grown on butter, wool, fat and bees-wax. Walker and Sweeney (35) describe morphological and tinctorial transmutations of the leprosy bacillus, and Eberson (36) discusses substantially the same changes regarding the general group of diphtheroids. McJunkin (37) has discovered a method of rendering living tubercle bacilli non-acid-fast through the action of dehydration and acetone or olive oil. The subject which once may have seemed simple is as yet in need of much explanation. Certainly all bacteria are not acid-fast by virtue of their waxy or lipoidal nature.

## SUMMARY

1. An acid-fast organism, morphologically similar to the tubercle bacillus, was found in kidney-pelves washings as the result of their growing in the urological irrigating apparatus, in spite of the presence of mercury-cyanide solutions. This organism almost completely lost its

acid-fast reaction on ordinary culture media and regained it only when subcultured on rubber tubing. Its other characteristics are listed.

2. The discussion concerns the distribution, isolation, identification and classification of the saprophytic mycobacteria.

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# SPONTANEOUS PNEUMOTHORAX (RUPTURE OF THE LUNG) WITH ABDOMINAL SYMPTOMS IN THE COURSE OF ARTIFICIAL PNEUMOTHORAX

**A Report of 2 Cases**

MARK H. JORESS[1]

The occurrence of spontaneous pneumothorax in tuberculosis is one of the dramatic incidents in this disease (1). The symptoms accompanying this complication vary in severity, depending upon the rapidity with which air enters the pleural sac inducing collapse of the underlying lung. In the event that a massive pneumothorax has taken place, symptoms are apt to appear with marked suddenness.

The outstanding symptoms of a full-fledged spontaneous pneumothorax are as follows: Severe pain in the affected side of the chest, marked dyspnoea, fever and shock. The most conspicuous manifestation of the entire symptom-complex is the appearance and persistence of dyspnoea. The latter, in particular, makes the medical attendant suspect that a perforation through and collapse of the lung have taken place.

In this communication the writer wishes to present a study of 2 cases of spontaneous pneumothorax with unusual manifestations. The cases to be described are unique for the following reasons: one, the spontaneous pneumothorax in each case occurred as a complication of a well-established artificial pneumothorax; and, two, the symptomatology in each case pointed away from the thorax as the site of trouble.

## *Case Reports*

*1:* D. B., female, age 26. First seen by writer in April, 1931, and diagnosed as chronic, fibrocavernous tuberculosis of left upper lobe, with chronic fibroid right apex. There was a past history of haemoptysis, and marked toxaemia was present at time of first examination.

In view of the destructive, progressive lesion over the left side, it was decided to institute artificial-pneumothorax therapy, which was started a month later. The patient responded well to compression from the start. At the end of a 5-month period the temperature had reached a normal level, sputum was scanty and nonbacillary, and patient was on light exercise.

[1] Boston, Massachusetts.

Difficulties began, however, one day, about 5 days after a preceding refill. The patient became violently ill, with excruciating abdominal pain radiating to the left flank, to be followed by nausea and vomiting soon afterward. The pain continued during the next 52 hours, radiating to the left loin on the third day. At this time the patient was seen by a surgical consultant whose opinion was as follows: "A surgical abdomen is to be considered, yet further observation is indicated."

Abdominal pain continued for 5 days, at the end of which it became less severe. Pain in the abdomen was still present. Chest signs were not yet consistent, however, with a massive pneumothorax. Although the latter was at times thought of, it was not given serious consideration because of the striking abdominal symptomatology. At the end of the 5th day radiography revealed the true nature of the trouble,—an extensive left-sided pneumothorax, the end-result of a rupture of the lung. A pleural exudate appeared during the next few days, and the patient's condition began to improve. The abdominal symptoms gradually disappeared and the patient began to feel well again during the ensuing weeks.

*2:* A.M., age 34, male. Was seen by writer for first time in January, 1933. The patient presented at that time a caseating, cavernous tuberculosis, involving the right upper and middle lobes. Patient's general condition was poor; there was much pallor and toxaemia. Sputum was 2 to 3 ounces in 24 hours, and bacillary. Patient was febrile each day to 100°–101°F.

Following a preliminary period of 8 weeks of bed-rest, artificial pneumothorax was induced. Patient did well from the start. At the end of a 14-month period of continuous compression, he had regained his strength and weight; sputum became scanty and nonbacillary; and patient was able to take light exercise, and do chores about the house without difficulty.

As stated, all went well until one day, two weeks following a preceding refill and about fourteen months after compression was begun, upon returning home from a customary walk, patient complained of not feeling well. He developed fever and malaise, and was markedly prostrated. In addition, he complained of soreness over the right costal margin. There was no dyspnoea present, and physical examination did not point to anything abnormal within the chest to make one think of intrathoracic disease. The diagnosis at the beginning of the illness, as well as during the ensuing period of three weeks, was that of the grippe. However, abdominal manifestations of what later appeared to be symptoms of a spontaneous pneumothorax became manifest at the end of this prodromal period. At this time there appeared generalized abdominal pain, radiating to the right hypochondrium, nausea and vomiting.

However, despite the lack of dyspnoea in this case, examination of the chest at this time made the writer suspect the presence of a spontaneous pneumothorax. To verify this suspicion, the pneumothorax apparatus was adjusted

as for a refill. The initial pressure was found to be positive, and, following the introduction of 100 cc. of atmospheric air the intrapleural pressure became still more positive. This observation confirmed the suspicion entertained prior to performing the test inflation. Air-aspiration was decided upon, and 700 cc. of air was withdrawn, with immediate relief of abdominal symptoms.

## DISCUSSION

In the first case the symptoms were abdominal in localization from the start. The clinical picture was so classical of acute intraäbdominal disease that a tentative diagnosis of a "surgical abdomen" was made. The true nature of the trouble was revealed only after radiography of the chest was carried out.

The second case, too, presented abdominal symptoms, and the classical symptom of dyspnoea was absent. But the situation here was more complicated, since the frank abdominal symptom-complex was preceded by a vague, prodromal period which lasted about three weeks. During this antecendent period the patient exhibited symptoms consistent with those of the grippe. In this case, however, a spontaneous pneumothorax was suspected. A test pleural puncture was done to corroborate the suspicion of a lung-rupture, with relief of symptoms following the aspiration of 700 cc. of air.

The cases just described are examples of how unorthodox may be the symptomatology accompanying a spontaneous pneumothorax. In this condition the symptoms are, as a rule, confined to the thorax. However, in the patients just discussed, the symptoms of chest pain and dyspnoea were entirely absent throughout their illness. In fact, the symptoms in these cases were abdominal in distribution, and pointed away from the thorax, the true seat of disease.

## CONCLUSIONS

1. Observations made on the cases reported in this paper point to a serious clinical entity which may be overlooked in cases receiving artificial pneumothorax.

2. Although spontaneous pneumothorax complicating induced compression therapy is generally easy to diagnose, in the absence of thoracic symptomatology a diagnosis of lung-rupture may be difficult.

3. Attention is directed to the appearance of abdominal symptoms in 2 cases of spontaneous pneumothorax, diagnosed in one instance by the use of radiography, and in a second by the use of a test pleural puncture.

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# TANNIN TREATMENT IN TUBERCULOSIS

## A Preliminary Report

S. LOUMOS AND S. H. ROSENBLUM[1]

The use of tannin in the treatment of tuberculosis is not new. Several decades ago the French particularly used tannic acid in the treatment of pulmonary tuberculosis as a tonic and antisudoric, and, in combination with iodine, it was regarded as specific in the treatment of surgical tuberculosis, especially in scrofula and tuberculous lymph nodes (1). During the last decade further attention was called to this treatment, and tannin was studied more extensively. Küss (2) made interesting experiments on pigs, showing the usefulness of tannin. In experimental tuberculosis with animals treated with tannin, he observed the tuberculous lesions as less advanced, and the animals remaining in better condition than the controls. According to Küss, tannin affects the "terrain" and renders it less favorable to the dissemination of the bacilli. It facilitates bronchial drainage, and favors the resolution of perituberculous congestion; and from this point of view it is useful in haemorrhage. The tannic acid was used by the French clinicians (3) (4) by mouth and was claimed to be useful in selected cases. Unfortunately, it causes gastric disturbances, and its use becomes difficult and annoying.

Lately the Russian, Shakhtakhtinskiy (5), used another kind of tannin, named *pistacia-red*, hypodermically, in solution of 0.5 per cent, 1 to 2 cc., on alternate days and claimed miraculous results. He reported 487 cases of pulmonary tuberculosis and 61 cases of surgical tuberculosis treated with this substance. The majority of the pulmonary cases were far advanced, in both active and inactive forms. Shortly after beginning the treatment, the patients became afebrile, perspiration decreased, appetite improved, and there was considerable gain in weight. Roentgenological findings showed that the exudative processes became more productive and then underwent fibrosis. In some cases the changes occurred more slowly. The number of the given injections were between 20 (in early tuberculosis) up to 38 in severe cases. According to this author, tannin products, similar to "neurotropic" and "lipotropic" dyes,

[1] Chicago, Illinois.

are usually "mesenchymotropic" substances. The tubercle presents a new formation from connective-tissue elements. It is known that tannin substances prevent decomposition of the connective tissue. Therefore, if they are introduced into the tubercle, the usual process is interfered with. The course of the tubercle may be altered, so that fibrosis becomes predominant. In relation to many bacteria, many of the tannin substances have powerful disinfecting and antiseptic properties, and this fact is very significant, as it prevents the development of bacteria. The above observations, such as clinical and experimental, led one of us (S. L.) to try tannin in the treatment of tuberculosis. The method was used on patients at the Cook County Tuberculosis Hospital. Sodium tannate was used hypodermically in a solution of 0.5 per cent on alternate days in the intrascapular region. The sodium tannate was preferred because "the systemic action of tannin is chiefly that of the alkali tannates, probably the only effective form which can exist in the blood" (Pharma-Kohen). For that reason we used sodium tannate directly.

Twenty unselected cases were treated. Nineteen were pulmonary cases and one lymphatic. The patients have taken tannin from two and a half to five months so far. The results of this treatment are as follows: In six of the cases the treatment failed to show any results. These cases were progressive and very probably in some of them the medication activated the process. In these cases the treatment was discontinued in the fourth or sixth week. In the other 13 cases, six presented cavities and seven showed more or less infiltration. All of them improved somewhat. Nine showed definite improvement clinically, progressive increase of weight, less expectoration, increase of appetite and strength, and the râles became less pronounced. In the other four, while there was no increase in weight, the general condition improved as well as the appetite and strength, and the pulmonary findings became less pronounced. In 7 cases the roentgenological findings improved definitely. Of these 13 cases, three were slow, progressive, febrile cases; the fever in one disappeared after four months of treatment and in the other two became lowered. Four cases were improving slowly before the treatment but after that they improved rapidly. Six cases were stationary for several months and started to improve after the treatment.

In 11 cases, while the expectoration was diminished, the sputum remained variable; in two the sputum became negative after three months' treatment.

Concerning the dosage, a 1 per cent solution was tried in the failing

cases, without result. However, this medication was entirely harmless. There was no reaction, either local or systemic, even in patients who took 50 injections during the treatment.

In one case of bilateral cervical lymphadenitis, an increase of the discharge was observed in the beginning of treatment, followed by a lessening and finally disappearance after 20 injections; 1 cc. of the solution had been given on alternate days. At the same time, in the enlarged lymph nodes without suppuration, a rapid swelling and suppuration were observed. Because of this reaction, the injections were discontinued and the sodium tannate was given by mouth with iodine, another specific for tuberculous lymph nodes. The amount given was 0.15 sodium tannate and 0.10 iodine daily, made in the form of a syrup. In this way reactions were avoided. One of us (S. L.) used this method in many cases of scrofula and enlarged lymph nodes in private practice with excellent results. The lymph nodes are dissolved without suppuration and the patients (mostly children) gain weight. One patient, treated for pulmonary tuberculosis, was also suffering with a fistula-in-ano which was greatly improved.

*Case Reports*

*1:* P. S., age 15, Mexican, female, single. Admitted May 4, 1935; both lungs involved; a far-advanced case. Sputum positive; temperature from 102° to 103°; pulse 116 to 130. Poor prognosis given on admission. Slow improvement started on June 1, 1934, but more marked after the beginning of sodium-tannate treatment in two and a half months; sputum negative.

*2:* G. S., age 20, colored, female; admitted July 22, 1935, as far-advanced case with bilateral involvement, more pronounced on left side. Temperature ranged from 98° to 101°. Poor prognosis offered. Bilateral pneumothorax was attempted, but had to be abandoned soon because patient could not stand the dyspnoea and pain. Improvement started one month after beginning of treatment; sputum still positive. Runs only occasional temperature as high as 99.4°.

*3:* Mr. M. J., 31, colored, admitted July 20, 1933. Far-advanced case with temperature of 100° to 102°. Prognosis poor. Wassermann, plus 4; sputum positive. Also had a fistula-in-ano. Patient picked up some weight, and temperature subsided somewhat after several months' stay in the hospital. He soon failed again, and it was thought that he would die. In October, 1934, he began to improve; his temperature ranged from 99° to 101°; treatment of

sodium tannate was started, December 1, 1934. Since then he has improved rapidly and is now afebrile, has gained considerable weight, and the fistula is improving; sputum is variable.

## SUMMARY

A 0.5 per cent solution of sodium tannate was used hypodermically in 19 unselected cases of pulmonary tuberculosis and in one case of lymph-node tuberculosis. In 6 cases of pulmonary tuberculosis the treatment failed to give any results. In the other thirteen a more or less marked improvement was observed. The discharging lymph nodes were improved quickly.

We are indebted to Dr. E. B. Freilich, Chief of Staff of the Cook County Tuberculosis Hospital, for his courtesy in permitting us to work with these patients.

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